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CLINICAL SENSE*

THE USE OF THE FIVE SENSES

BY

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Clinical knowledge depends upon three processes—observing, recording, and thinking. Each embodies a different use of the word sense. Observing requires a sense of perception—that is, skilled use of the senses; recording depends on the use of words in their correct sense—that is, the art of making sense; and thinking (which includes the processes of consideration, rumination, and deliberation) requires the use of a third kind of sense—the opposite of nonsense—a sense of wisdom. These three kinds of sense—perceptual sense, word sense, and common sense, growing from that one word, form a tripod which supports the whole structure of clinical medicine. In other words the art of medicine depends on the stimuli that enter the mind of the physician (or that structure corresponding to it in the surgeon), the processes that go on in that mind, and the resulting material produced by it.

The stimuli enter by the five senses of perception. The recording and transmission of those stimuli largely depends on the use of words, which, according to their suitability and their arrangement, have a far greater influence on medical progress than is generally recognized. After which the processes going on in the mind, deliberations, rejections and ponderings, depend on sense: sense of perspective, sense of reality, sense of logic, plain sense, common sense, and even horse sense. Is sense of humour a necessity? No, it is not essential; but, like a catalyst, it facilitates and enhances the process; like a flavouring agent, without being essential, it gives taste to an otherwise unassimilable bolus of knowledge. Like the use of catalysts or flavouring agents the use of humour must be restricted, or it will interfere with what it should enhance.

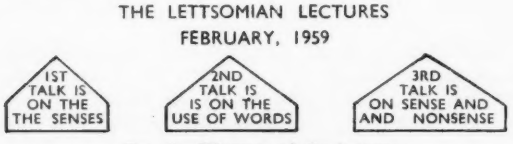
THE LETTSOMIAN LECTURES
FEBRUARY, 1959
1ST TALK IS ON THE THE SENSES
2ND TALK IS IS ON THE USE OF WORDS
3RD TALK IS ON SENSE AND AND NONSENSE

FIG. 1.—Diagram of the lectures.

The theme of my three lectures, in blunt phrases, can be summarized thus: Lecture 1: Use your eyes. Lecture 2: Use your tongue. Lecture 3: Use your loaf. I also present my theme in a diagram (Fig. 1) which you must study carefully, for I refer to it later.

This first lecture is to do with the five senses. Though I shall take them singly, I am sure they are rarely, if ever, used in that way. The clinician, when he tries to find what evil is causing the illness, does not say, "I see some evil," "I hear some evil," "I feel some evil." There are not three distinct processes. They are

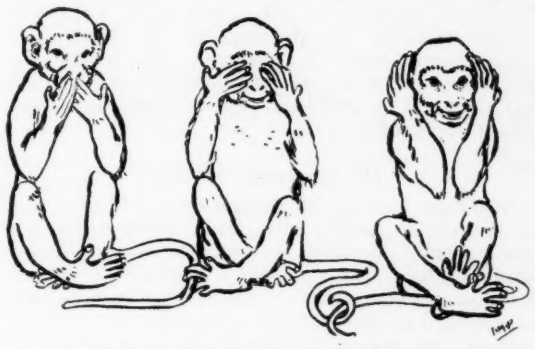

FIG. 2.—Speak no evil. See no evil. Hear no evil.

not separated like those three well-known monkeys (Fig. 2) who, by covering appropriate organs, arrived at the virtuous conclusions they desired. They are carried out simultaneously, supplemented by the helpful but less informative senses of taste and smell. Yet the methods depicted by those monkeys are widely used by most clinicians. We shut our eyes to observations which do not agree with our ideas. We close our ears to bits of history which seem out of place, or to noises coming down our stethoscopes which are not included in our catalogue of official sounds. We refrain from speaking about our observations when they are not listed in official textbook descriptions; we refrain from

FIG. 3.—Hidden man.

*The first of three Lettsomian Lectures, delivered at the Medical Society of London on February 9, 1959. The 2nd and 3rd Lectures, "Making Sense" and "Talking Sense," appeared in the *Lancet* of September 19 and 26, 1959. The complete trio "Sense and Sensibility" was published in The Medical Society's Transactions (*Lancet*, 1959, **2**, 359 and 417; *Trans. med. Soc.*, **75**, 66).

voicing our opinions when they conflict with current thought, or are greatly at variance with the opinions of those we fear. It is probably to our advantage that we do so, but it does not help the forward march of medical science.

In using our sense organs we see what we ought to see rather than what is there. We see what we expect, and unconsciously dismiss the anomalous. I illustrate this by referring back to Fig. 1. In that diagram there are three deliberate mistakes; three entirely wrong words, but those of you who have been fitted with efficient suppressors may have seen none of them. The clinician is both blessed and cursed with this suppressive mechanism—blessed when he detects a significant pattern, but cursed when important trivialities are tidied away without being appreciated. The recognition of significant patterns depends on experience and education. Fig. 3 shows a pattern which is meaningless to those who are inexperienced or uneducated (by which I mean the majority of this audience). Yet if it is shown alongside a picture which teaches you what to see (Fig. 4), you will quickly acquire the skill of interpretation. Now look again at the old pattern (Fig. 3) and you cannot help but see the face of the man. You unconsciously select the relevant, and eschew the irrelevant; you dismiss the meaningless squiggles in the periphery and see only those that experience has taught you to recognize as a man's face.

The Suppressive Faculty

When the experienced clinician takes a history from a loquacious patient, the many irrelevancies are unconsciously dismissed, like the meaningless squiggles in the picture. This suppressive faculty, by producing selective deafness, selective blindness, and other sense rejections, can easily suppress significant or relevant things. The patient with attacks of acute abdominal pain may not be heard while she is describing the chronic rheumatism in her legs, but that very symptom can be the most important clue to the origin of her abdominal pains, because her "rheumatism" consists of acute lancinating pains like red-hot needles being jabbed into her. When her lightning pains are appreciated, it is easy to diagnose the abdominal pains as the gastric crises of tabes dorsalis. That is not an imaginary case. Two laparotomy scars witness to its truth.

Suppression of sight can be no less important. Fig. 5 shows the conventional nuclear shapes of neutrophil leucocytes we found in our textbooks, but many years of microscopy passed before anyone noticed the little drumstick-shaped appendages shown in Figs. 6 and 7. They were there when we looked at blood films as students, but none of us noticed them, nor were they drawn in many of our textbooks. Davidson and Robertson Smith (1954) pointed out that these drumsticks occur only in women, and thus discovered a method of distinguishing female blood from that of males which was so accurate that they correctly foretold the sex in 50 consecutive blood films.

FIG. 4.—Discovered man and hidden man.

It appears that what we see depends not so much on the acuity of our vision as on what we have been taught to see. Sir Francis Galton performed experiments with sailors to find out why they could see a distant mooring buoy when a landlubber could not do so, and showed that the weather-beaten eyes of the sailor were much less sharp sighted than those of the man from the land.

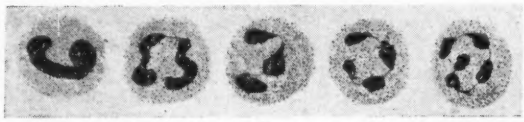

FIG. 5.—Cells of the different groups in the Cooke counts (Whitby and Britton, 1957)

FIG. 6

FIG. 7

FIG. 6.—The characteristic drumstick found in the female neutrophil leucocyte. The thin strand of chromatin joining the head to a nuclear lobe can be seen clearly. (Jenner-Giemsa. ×1,750.) (Davidson and Smith, 1954). FIG. 7.—A female neutrophil showing a bilobed nucleus. Projecting from the left lobe is a characteristic drumstick, and immediately to its right, connecting the two lobes, is a minor lobe. Two trivial projections from the right main lobe are "small clubs." (Jenner-Giemsa. ×1,750.) (Davidson and Smith, 1954).

The visual stimuli reached the retina of the landsman more accurately than they did in the seaman, but did not register at the cortical level. The inexperienced man from the land saw, but he did not notice; he perceived without recognizing, just as you could not recognize the face in the early picture though it was there for you to see, and you failed to see the redundant words in the first diagram because your brains tidied away these irrelevancies without your being conscious of it.

Thus clinical acumen does not vary with acuteness of the senses, though such acuteness is an advantage. The medical student who misses an aortic diastolic murmur almost certainly has better hearing than the consultant who teaches him to recognize it. Clinical acumen largely depends on the unconscious selection and rejection of sensory stimuli. In the plainer words of Polynesia, the parrot who belonged to that legendary clinician Dr. Doolittle, it depends upon being a good noticer.

The Gift of "Noticing"

Two special kinds of noticing occur in the highest form of geniuses and in pioneers. The ability to notice the significance of what seems to be irrelevant, and the ability to detect what is common to several groups of data. An example of the first faculty is Sir Alexander

Fleming's enlightened scrutiny of the penicillin mould which polluted one of his culture plates. Trivialities like that might fall on a million sense-organs before they blossomed into interpretation.

A special word for this faculty—serendipity, was coined by Horace Walpole in 1754 and defined as "the faculty of making happy and unexpected discoveries by accident"; but luck alone is not enough. You need to be a good noticer. Jane Austen wrote in *Emma*: "Depend upon it, a lucky guess is never merely luck, there is always some talent in it."

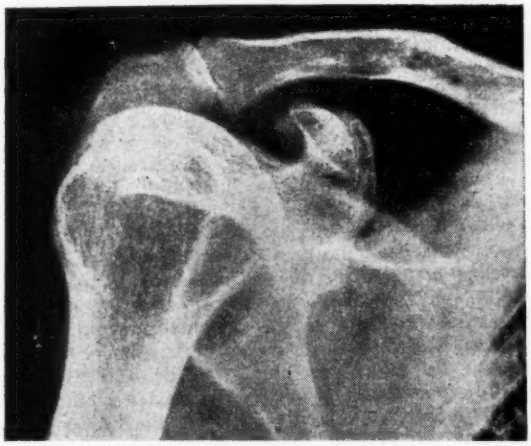

FIG. 8.—*X*-ray film of injured shoulder-joint, also showing a portion of lung.

To illustrate serendipity I show the *x*-ray film of a workman's shoulder, taken after he injured it at work (Fig. 8). As you see, it shows no bony injury. Look again and see if you notice anything wrong.

A little corner of lung is showing, and the late Dr. Whitehead, being fortunately serendipous, noticed it was abnormal and ordered a full-size *x*-ray film of the lungs. This remarkable appearance was then revealed (Fig. 9). This chance discovery (or rather chance wedded to perspicacity) led to the discovery of the pneumoconiosis caused by tin oxide dust, now known as "stannosis." Other workers at the same factory as this man had extensive changes, too, but because the condition produced no symptoms it remained unknown until this shoulder injury brought it to light. This gift of seeing the gold that glitters among the dross may depend upon negative observations; it includes what you do not see as well as what you do see, and what you do not hear as well as what you hear.

"May I call your attention to the singular incident of the dog in the night time," said Sherlock Holmes. "But the dog did nothing in the night time," said Dr. Watson. "That," said Holmes, "is the singular incident."

In 1897 Sir James Mackenzie was examining an old patient with mitral stenosis who had suddenly developed a rapid irregular action of the heart. He saw that there was no auricular wave in the jugular veins and he heard that there was no presystolic murmur. In fact, he heard and saw nothing. The auricle was doing nothing: that was the significant incident. That was how he discovered auricular fibrillation which he described then as paralysis of the auricle. He wrote: "For many years I speculated as to what the auricle was doing after it ceased to appear in the tracings; when Dr. Lewis adduced experimental proof that cessation of auricular activity was due to fibrillation I had no hesitation in accepting the term." Now we know the circus movement of Sir Thomas Lewis does not really take place, Sir James Mackenzie seems to have been quite near the mark with his term—paralysis. The absence of dental caries in fluoride-rich districts and the absence of smallpox among dairymaids are further examples of negative observations which led to enormous clinical advances. When the absence of coronary disease among Bantus is solved even a greater advance may be made.

The second faculty of seeing what is common to apparently dissimilar patterns is of incalculable value, not only in clinical medicine, but also in passing the eleven-plus examination, where a familiar type of question is: "Which of these have something in common," followed by a diagram or a series of figures.

The first stage in an important clinical discovery is often the observation that a series of puzzling cases, though differing in many ways, possess one factor common to all. The commonest cause of infantile blindness to-day is retrolental fibroplasia, and till a few years ago its incidence was steadily rising. It was noticed that it occurred far more in children born prematurely: that was a factor, but not the highest common factor. The highest common factor was that not only were all the blind children premature, but they had all been given oxygen. The detection of this common factor has protected hundreds of children from blindness.

Here is another puzzling epidemic solved by "noticing" (Kinnear, 1948) a most unusual common factor. In 1947 there was an epidemic of bullous erythema in Dundee. All the cases were women, and all the lesions were situated in a band across the back of both calves in exactly the same place. There were no marks on the stockings, so chemical burns were excluded. At the height of the epidemic one particularly observant patient noticed that her attacks of

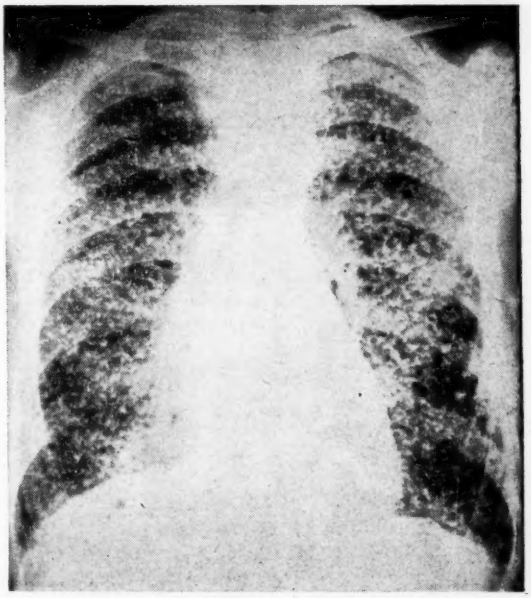

FIG. 9.—*X*-ray film of chest of patient in Fig. 8, showing stannosis.

blistering of the calf always came on a few hours after travelling on a particular tram route; she also recognized many other people affected by the epidemic as fellow travellers on this route. A careful inspection of all the trams was made, and it was found that one tram was responsible for the entire outbreak. In this vehicle there was a longitudinal groove in the slat of wood which held the seats in place. In this groove there was a thriving colony of bed bugs, just where the women's calves touched the wood when they sat down. It was clear that these bugs had reversed their normal mode of life, lying hidden at night when the tram was in the garage, and by day sitting in a row, feeding from the bounteous and constantly changing supply of calves presented to them. The tram was disinfested, the groove planed out, and the epidemic ended abruptly.

The recognition of something common to several patients constitutes a similar kind of clinical sense.

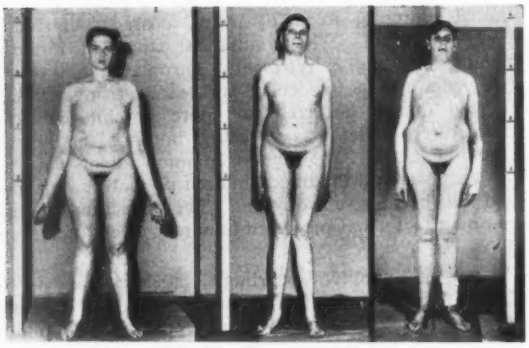

FIG. 10.—Three eunuchs.

FIG. 11.—Patient with myxoedema huddling under a mound of bedclothes.

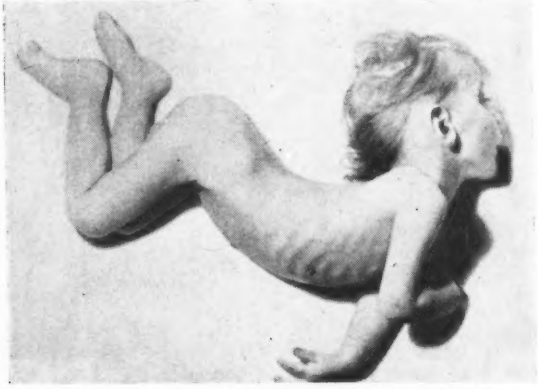

FIG. 12.—The "gun hammer" position in meningitis.

Anybody who has seen several mongols or a number of patients with myxoedema soon realizes that though individual cases differ widely there is something common to all of them. It is hard to name, but, like a family likeness, extends throughout the group. Fig. 10 shows this kind of common factor. The three eunuchoids in the photograph all look quite different and yet clearly resemble each other because of a common factor (testicular hormone deficiency).

So far I have discussed the collective use of the senses: the selection of sense data, the exclusion of irrelevant stimuli, the recognition of familiar patterns and common factors. I now pass to the individual use of the senses.

Sight

Without doubt sight takes first place. The number of clinical data that can be seen is far greater than is available to the other senses. We see colour, shape, movement, position, expression, and a hundred-and-one indefinables. I will mention a few of each, starting with the colour of the face: the plum colour of polycythaemia; the ruby colour of the alcoholic; the yellow colour of pernicious anaemia; and the cyanosis of congenital heart disease with arteriovenous shunt or that produced by inexperienced anaesthetists. I think Keats must have seen anaesthetic cyanosis when he wrote the lines: "With beaded bubbles winking at the brim and purple stained mouth." We also recognize different colours in the urine: (*a*) the yellow of normal urine, (*b*) the rose colour of anthocyanuria, (*c*) the iridescent pink of eosinuria, (*d*) the opalescent pink of haematuria, and (*e*) the greenish-blue colour of the urine when a patient is taking de Witt's kidney and bladder pills, which contain methylene blue.

We distinguish shapes, too—the shape of the hands in acromegaly, the hands of arachnodactyly, and the deformed head of hydrocephalus.*

Movements

We also learn much by observing movements: the gaits of congenital disease of the hip, and Parkinson's disease; the different ataxias of loss of position sense and loss of co-ordination; the involuntary movements of Sydenham's chorea and Huntington's chorea; the different tremblings of Graves's disease, Parkinsonism, and alcoholism. There are many other unnamed movements that enlighten the clinician: the restless plucking at the bedclothes called carphology, alleged to be typical of typhoid delirium, but far commoner in senile dementia or blindness; the restless head-turning and lip-smacking of the man with a bleeding-ulcer, and the informative movements made by patients while they give a history; the single pointing finger of the man with peptic-ulcer pain; the circulating spread-out hand of the man with colic, and the sponge-squeezing hands approaching the sternum of patients describing the pain of cardiac ischaemia—a movement that is almost diagnostic of coronary disease. Dr. Byron Evans first called my attention to it.

Position

The position of a patient in bed (the decubitus) can be highly informative; for example, in myxoedema—huddling under a mound of bedclothes (Fig. 11); or in

*During the lecture a series of lantern slides showed the various colours and shapes mentioned in the text.

meningitis—with head flung back (Fig. 12). A common, but little-known, decubitus is that found after a stroke, where the fact that one arm is under the bedclothes and the other outside, coupled with the well-known rotation of the head away from the paralysed side, may reveal a diagnosis missed on routine examination; this position is often found even in quite mild hemiparesis.

Though nobody has dignified the sitting position with a name, the deseditus, as it could be called, may be equally revealing. When a patient is giving a history her anxiety can be measured roughly by the distance of her sacrum from the back of the chair. As anxiety mounts so does the distance increase until she is perched on the edge in imminent danger. I once impressed my houseman by solving a mysterious case of P.U.O. purely by means of the deseditus. Ten days' high fever had followed a straightforward pneumonia, although the chest had cleared after penicillin. As I encountered this lady on my round I noticed she was sitting crookedly in her bed, and I asked her why. "I've got a pain here," she said, and rolled over to display a large abscess of the buttocks caused by a contaminated penicillin injection. This was literally the seat of the trouble.

FIG. 13.—Patient with institutional neurosis.

While talking about the value of posture in diagnosis, I wish to describe the characteristic posture which occurs in a dreadful disease of which I have only recently become aware. It is an old disease which most physicians have encountered, but, until Dr. Russell Barton pointed out to me the characteristic posture and told me his views about its causes and treatment, I had observed it without being properly aware of its significance. Figs. 13 and 14 show patients suffering from this condition. Can you recognize it? It is institutional neurosis—that syndrome of submissiveness, isolation, loss of individuality, automaton-like rigidity, and loss of all initiative which occurs in people who have been in institutions for a long while. If it occurs in a mental hospital it is often believed to be an end-result of mental illness. This is not so. This dreadful thing is caused by institutional life and nothing more. It is not confined to mental hospitals, but is found all over the world in orphanages, prisons, convents, homes for displaced persons, prisoner-of-war camps, and the chronic wards of municipal hospitals.

Because this disease has a characteristic posture, I include it in the use of sight in diagnosis. If I say more about it than other diseases with characteristic postures, it is because I believe it is less well-recognized than the other illnesses I have mentioned.

People afflicted by this man-made disease have no resentment at what has been done to them; indeed, when the disease has got its grip on them they often resent efforts made to cure it. They are not interested in the future; they have developed a resigned acceptance that everything will go on as it is (Fig. 15): inevitably, unchangingly, and indefinitely.

Characteristically, the hands are held across the body or tucked behind an apron, the shoulders are drooped, and the head is held forward. Entries in the notes, if any are kept, give further confirmation of the diagnosis thus: "Dull, apathetic, and childish" . . . "Mute, dirty, and withdrawn"; or alternatively, "Has settled down well" or "Is co-operative, and gives no trouble."

The causes of this illness are: (1) lack of contact with the outside world; (2) enforced idleness; (3) lack of personal possessions; (4) regimentation by nursing staff; (5) drab, colourless institution atmosphere; (6) absence of prospects outside the institution; (7) excessive sedation.

FIG. 14.—Another patient with institutional neurosis.

FIG. 15.—Patients showing resigned acceptance of institutional life.

Though mostly afflicting those who lack initiative and energy, the illness is not a primary condition. It can be prevented and it can be cured, but this needs unflagging energy and strength of purpose in those concerned.

I am greatly indebted to Dr. Russell Barton for telling me about this disease. Both the facts about it and these pictures illustrating it come from his monograph on Institutional Neurosis.

I will only refer to expression briefly because I have discussed it here* before. Fig. 16 captures the profound misery of melancholia, a diagnosis supported by the neck scars from a past attempt at suicide. Fig. 17 shows the cold smile of schizophrenia — remote, childish and eerie.

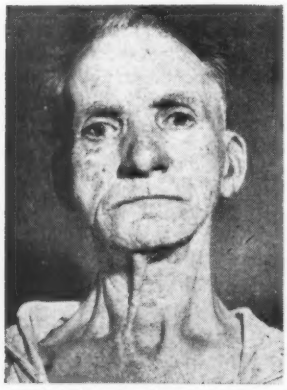

FIG. 16.—The profound misery of melancholia.

FIG. 17.—The cold smile of schizophrenia.

Hearing

Hearing is next in importance. I only consider the use of the naked ear unaided by instruments.

The most important sound heard by a clinician is the voice of his patient. With myxoedema, the quality of the voice may be more diagnostic than the history related by that voice; it is low and thick and slow, with a croaking fumbling quality that is unmistakable.

The speech may be clinically diagnostic in cleft-palate, diphtheritic palatal palsy, and myasthenia gravis; the myasthenic voice shows weakness and increasing nasal intonation as speech tires the palatal muscles The immediate change after an injection of neostigmine is one of the most dramatic sound-changes in medicine. Slurred speech, classically described in G.P.I., is rarely diagnostic, because it may be caused by drunkenness, a sore tongue, or only slovenly articulation. A distressingly slurred, spastic speech, painfully crawling from one word to another, may be heard in disseminated sclerosis.

A cough may be as revealing as the voice: the short painful cough of lobar pneumonia; the unique cough of pertussis—a diminuendo trail of little coughs with an apnoeic climax followed by the unmistakable, unforgettable whoop; and, commonest of all, the familiar sound of chronic bronchitis.

The sound of breathing does not need a stethoscope to hear it. The expiratory sibilant wheeze of asthma, the short jerky breaths of pneumonia, the deep slow breathing of diabetic coma; and lastly, that strange monotonous cycle of Cheyne–Stokes respiration; pianissimo, crescendo, fortissimo, diminuendo, pianissimo, tacet, da capo al fine ad infinitum.

Snoring usually signifies little; it is independent of the depth of sleep, occurring often during a light doze. But loud snoring in a hitherto silent sleeper is a little-recognized symptom of myxoedema, and its disappearance after treatment with thyroid is not only gratifying to the patient and her husband but a help in confirming the diagnosis.†

On rare occasions noises originating from the chest and the heart can be heard at the bedside without any amplification.

William Bean (1954) collected some striking examples of sounds heard at a distance from the chest. One patient, who had a pneumo-pericardium after acute pericarditis, developed such a loud exocardial murmur that it not only prevented him sleeping but also kept his wife awake; she had to sleep in another room. Another case of pneumo-pericardium reported by Bean had a more unusual cause (though the sound effects were similar). It followed a careless performance by a professional sword-swallower. Other patients who developed sudden noises in their chests had ruptured aortic valves, a condition that usually occurs when sudden exertion is performed by a man with diseased aortic valves. A man moving a piano downstairs suddenly felt something "go" in his chest, and those around him immediately heard a noise like that made by a young frog. Another man, while engaged in a drunken brawl, was interrupted by a sudden cooing noise like that of doves. In this case, too, the patient's wife complained of the noise at night, despite its traditionally soothing quality.

The most dramatically audible case of ruptured aortic valve was told me at the lunch-table by my friend Dr. Keith Ball. His patient also felt something "go" while he was doing heavy work in a saw-pit, and his work-mates assisted him home with a sound of machinery coming from his praecordium, a sound so loud that his wife heard it from her front room and came to see what was going on.

Loud endogenous noises are rarely of great diagnostic help, but Allen reported a lady with obscure anaemia who developed a rhythmic splashing sound like a water-mill which led to the discovery of a large hiatus hernia which had caused her anaemia. The churning noises were caused by her heart beating against the intrathoracic stomach.

I became interested in the subject when I was convalescing from virus pneumonia which was complicated by a physician exploring my chest for non-existent pus; this gave me a moderate-sized pneumothorax. Five days later, when I was beginning to get my breath back, I became conscious of a satisfying, twanging sensation arising from my left chest accompanied by a loud click, which I heard quite easily. To my delight two hospital doctors came to see me shortly afterwards and I made them stand at the foot of my bed and

*Asher, R. Face Values, *Trans. med. Soc.*, 1957, **73**, 48.

†During the lecture tape recordings were played to illustrate the voice changes, coughs, and breathing noises referred to in the text.

solemnly witness that they could hear my heart beating from where they stood. I was twanging away like a rather loud clock. The sound lasted for two or three days; I found it was loudest when I held my breath about three-quarters way through inspiration and lay tilted towards my right. I thought at first that I was unique, but I soon learned that spontaneous pneumothorax is a common cause of cardiac noises audible at a distance. I have not heard of iatrogenic pneumothorax being reported in this context, perhaps because those "iatres" who puncture the lung are not anxious to publish their work.

Another sound easily heard without a stethoscope is the splashing noise of a hydropneumothorax. The patient himself will often comment on it because he perceives an internal turbulence of rushing waters within his chest; he can feel as well as hear it. One of my patients with a hydropneumothorax complained that when he cleaned his teeth he felt like a human launderette. The vigorous lateral movement as he plied his toothbrush had the same effect as the clinician eliciting the sign gets by vigorously shaking the patient.

When I was a student the late Dr. Theodore Thompson told of a hunting squire with a chronic hydropneumothorax who regularly hunted three days a week. The only noticeable result of this action was that whenever he jumped a hedge the rest of the hunt thought he had landed in a ditch because of the splashing of mighty waters which accompanied his descent. Soon after Dr. Thompson taught me these interesting hydro-acoustics one of my cases appeared to be suffering from hydropneumothorax. I can still remember the ward-sister watching with mild astonishment as I seized the frail young man and shook him to and fro. To my delight there came an unmistakable gurgling and splashing. As I was glorying in this diagnostic *tour-de-force,* the sister asked me quietly: "Would you like me to take this bottle out of the bed, doctor? It's making rather a mess."

Everybody knows that noises from the abdomen are often audible outside, but, except for the borborygmi of carcinoid tumour, their importance is social rather than clinical. It is the absence of borborygmi rather than their presence which is significant, and a belly which is silent even to the inquiring stethoscope is likely to contain paralysed intestines. The most startling noise that ever comes from the abdomen is the cry of an unborn child. Numerous cases are reported when everybody in the obstetric theatre has distinctly heard the cry of the intrauterine child. The sound is usually short and muffled, but Livy reported that an infant of the Marrucini, while yet unborn, cried out in a loud voice from his mother's womb: "Io triumphe," which roughly translated means "whoopee." This case is not so well attested as the earlier examples to which I referred.

Noises from joints are often and easily heard, so they should be mentioned here, but they have very little clinical value. A joint is capable of producing a great deal of noise with little disability. Another joint may be extremely painful on movement and yet produce no sound. All the same, I believe noisy joints are more commonly diseased than silent ones are, and a noisy joint is more likely to be the site of osteo-arthritis than rheumatoid arthritis. The sound made by moving a Charcot joint is supposed to resemble that of crunching snow; it is the feel of this noise rather than the sound of it which is characteristic, just as the sound produced by walking on crunching snow is felt through the boots as well as heard in the ears.

As percussion of the chest involves unaided hearing, it deserves to be considered here. There is no doubt that stony dullness is a reliable indication of the presence of fluid: careful percussion of the chest may reveal fluid better than the chest *x*-ray film does. When there is little radiological evidence of fluid, but the percussion note is stony-dull in one place, then it is well worth aspirating for fluid there. Though percussion is considered with the use of hearing there is as much justification for inserting it in the section on the use of touch. In stony dullness the sign can be felt as much in the finger as it can be heard with the ear, and more in the finger that is struck than in the striking finger.

I have difficulty in judging other grades of dullness. If I find that the right chest gives a less resonant note than the left, I would, if the history suggested right-sided pneumonia, consider there was an impaired percussion note on the right; whereas if the history suggested a left-sided pneumothorax I would accept that the left side was hyperresonant. Percussion gives me information about the relative resonances of the two sides rather than absolute information about one spot. I am aware that when one side is duller to percussion than the other I am sometimes only observing that the pitch of the note is higher and that both sides give an equally loud and equally resonant note. I doubt whether many clinicians can distinguish alterations in pitch, tone, and volume; and even if they could be trained to do so I do not think great benefit would accrue, because, except for stony dullness, there is so little constant relation between the change in percussion note and the disease beneath. On the vexed question of percussion of the heart, I was taught that if I ever found an area of cardiac dullness when percussing a heart then there was a pericardial effusion. I think that was sound teaching.

Touch

Touch is equal in value to hearing, and here I include all sensations detectable by the clinician's exploring hand. First, temperature. Although it is better to use a clinical thermometer than to place an old-fashioned hand on a fevered brow, quite often a clinician feeling the chest for expansion or palpating an abdomen for tenderness is struck by the abnormal warmth. The temperature may have been normal when the chart was filled in, and feeling the hot skin may convey an important change in temperature which might otherwise have been missed. The extra warmth of a bone affected by Paget's disease is also of diagnostic help. The feel of the skin in certain rare conditions can be diagnostic. In Cushing's syndrome the superficial layers of the skin can be pinched up separately, giving a sensation as if picking a thin fold of oilskin between the fingers. A grosser degree of skin levitation is both felt and seen in the rare familial Ehlers-Danlos syndrome.

In scleroderma the opposite obtains and the skin feels adherent, inelastic, and immobile. Alan Read, an ex-registrar of mine, pointed out to me that in facial scleroderma this shows when trying to inspect the

conjunctiva for anaemia. The lower lid will not turn down as it should. In gross myxoedema the combination of dryness, roughness, and corpse-like coldness gives the observer an unforgettable impression as if he were touching a lizard. In subcutaneous emphysema the sensation of palpating small amounts of air beneath the skin is strange and unique: the crinkling flickering tingle imparted to the finger-tips is both diagnostic and satisfying. The old physicians attached great importance to the feel of the pulse, perhaps exaggerating its importance, but the feel of a collapsing pulse remains a valuable sign, though it feels nothing like a water-hammer. Few clinicians have felt a water-hammer, and I am lucky to possess one. I admit I enjoy playing with it, but it feels nothing like a collapsing pulse.*

In feeling vibrations the palpating hand can gain much information because some sounds are easier to feel than to hear. The deeper notes are generally palpable, whereas the higher notes are audible. I have noticed that vocal fremitus may be decreased over solid lung even though the resonance is increased; this obtains when there is rather high-pitched aegophony. Fluid in the pleura seems to damp down the palpable vibrations which produce vocal fremitus, although breath sounds and vocal resonance are little diminished. To expect breath sounds to be absent over pleural fluid is a mistake.

In palpating cardiac vibrations the palm of the hand provides invaluable information. The low diastolic murmur of mitral stenosis may be felt as a thrill more easily than it is heard as a murmur. Not only can the diastolic murmur be felt, but the slapping first sound may be felt so clearly as well that the observer feels almost as if he heard the whole cardiac cycle with his palm.

I am interested in which part of the hand is most sensitive to thrills. I have conducted trials with many students and found it remarkably constant. In every one I have tested it has been sited as the junction of finger and palm, mostly on the palmar aspect of the metacarpal heads. Try moving your hand over a faint thrill and you will find that is where you will feel it most easily.

With grosser thrills there is no need for finesse, and any part of the body can feel it. In one unusual case I first noticed a thrill in my right knee. I was interviewing a chronic schizophrenic who had just told me that the B.B.C. were continuously transmitting radio vibrations throughout her body. As I approached her my knee touched the end of her bed, and I immediately felt the most intense vibration coming from her right leg, which was touching the bed-rail. She had multiple arteriovenous communications as a result of an accidental shot-gun wound several years previously. Her views about the B.B.C. were both inaccurate and coincidental.

Apart from vascular thrills there is the fluid thrill, an invaluable sign of ascites more reliable than shifting dullness. I doubt the need for a third party to partition the abdomen with the side of the hand, except when an examiner is watching. Nothing else but fluid can mimic the short flickering vibration which greets the left hand about one-third of a second after a light tap has been administered by the right. With hydroceles, too, the fluid vibration is diagnostic and reminiscent of the water-bombs we made in our childhood from balloons, or finger-stalls inflated with water.

Another thing that can be felt is the tone detected by manipulating a relaxed limb; the flaccid unresponsive tonelessness of a limb newly paralysed by a stroke is often the most informative sign in a deeply unconscious patient; when released from the observer's hold it drops with a dead-weight flop quite different from the more leisurely descent of its unparalysed counterpart. Detecting increased tone is more difficult. There is a difference between the feel of spastic hypertonus and wilful contraction, but it needs skill to distinguish it. I find that a normal patient (and even more so a subnormal patient), when asked to let his leg go loose while the examining hands gather the limb into position for the knee-jerk, immediately gives muscular contractions of tetanic strength which hold the limb as straight as a rod until, with a mixture of persuasion and Judo, the clinician manipulates it into the position he wants. Why the ability to let the limb go loose at will should be denied to all except those of the highest intellect is unknown to me, but I commend this observation as a possible screening test for selecting students.

The most valuable of manual sensibilities is that obtained by palpation when feeling for swellings, an entirely different thing from palpation for vibrations, though called by the same name. Here we are using a combination of touch, sense of position, deep pressure, and joint sense. We do not perceive a constant sensation, but a change. We cannot palpate except with movement. The movements required, whether for palpating axillary glands or for the detection of splenomegaly, are highly skilled and developed only by experience and instruction. They are not amenable to description in the lecture room; so I do not discuss the art of palpation except to say two things about palpation of the abdomen.

First, the convention of leaving the genitalia covered by bedclothes is kind to the patient but unhelpful to the clinician. The angle of the palpating hand is distorted by the heaped bedclothes. There is no elbow-room. The difference if all the bedclothes are pushed right back (leaving only a sheet if necessary) is remarkable.

The second thing is that in a warm bed patients relax much better than on an out-patient couch. I have noticed several times when I have admitted someone from the out-patient department that a few hours later I can feel much more than before, and find lumps which I had previously missed.

With instrumental manipulation much information is imparted by "the feel" given to the hands: the "give" of a needle as it enters a spinal theca or an antecubital vein; the satisfying snap of a dislocated shoulder returning to its place; and the particular resistance imparted to the instrument when a urethral stricture is encountered.

I suppose that judging weight ought to be included with information that can be felt. Quite small differences of weight can be detected. As I have an old-fashioned plate camera I find this faculty useful in deciding which of my plate-holders are loaded. But I can think of no clinical use for it, except that a carcinoma of the testis, it is said, can be distinguished from a gumma because of its greater weight. I can only

*The medical term "water-hammer" derives from its use in hydraulics to describe the concussion of moving fluid meeting still fluid in a pipe. A water-hammer pulse thus refers to the "slap" of resurgent blood in the artery and not to the laboratory instrument at all. (See *O.E.D.*)

remember encountering one gumma of the testis, and I cannot remember whether it felt light or heavy.

Taste

I remember about 10 years ago a baby had ascites of such milky whiteness that some of the wondering doctors thought it was milk which had leaked from a breach in the alimentary tract. Others believed it was chylous ascites secondary to blocking of the thoracic duct. Dr. John Humphrey, our biochemist, was called in to settle the problem. He looked thoughtfully at a specimen of the fluid for a few seconds, and then gravely took a generous sip. Without hesitation he shook his head and said: "That is not milk." That is the only time I recollect the faculty of taste being of clinical use. But Matthew Dobson (who, we know, was a member of this Society) wrote these words in 1776:

"*Experiment V.*—After evaporating two quarts of urine to dryness by gentle heat, there remained a white cake, which was granulated and broke easily between the fingers. It smelled like brown sugar, neither could it from the taste be distinguished from sugar."

That is the first time sugar was demonstrated in the urine of a diabetic, and provides a vivid example of the use of taste and smell in clinical science.

Smell

The range of olfactory stimuli is large, but the information they convey is relatively small. Alcoholic breath is easily recognized, but may be misleading in unconscious patients because it is often the associated head injury and not the alcohol which causes the stupor. Acetone in the breath in diabetic coma and in children who have been vomiting is easily detected by those who have the gift. I am not able to smell it at all, and yet if somebody is taking off nail polish with acetone two rooms away, I am in no doubt about it. There is no doubt some people can smell something in diabetic coma. Two months ago a child operated on for suspected appendicitis vomited over the anaesthetist, who commented on the strong smell of acetone, and so revealed that diabetic pre-coma was the cause of the abdominal pain.

Sir Eric Riches told me he does not believe that uraemia can be recognized by the smell of the breath, but the smell of urine inseparable from prostatic cases perpetuates the belief. I am convinced that this is true, for a continent patient dying of Bright's disease may have a grossly elevated blood urea with no uraemic smell about him. Has any scientific work identified the substances excreted in the breath of diabetics to establish which, if any, can be smelt. Is the acetone-like smell of diabetic breath due to acetone or some other volatile ester? Is the ability to smell this substance transmitted genetically like the abilities of "tasters" and "non-tasters" which are clearly distinguished by the use of phenylthiocarbamide? If the breath from patients with diabetic coma is bubbled through a liquid, will that liquid give a positive Rothera test? I am bothered that so little is known about these matters which might be settled experimentally, when other things of less moment are thoroughly investigated: for instance, it is well established that the urine of patients with the Lawrence–Moon–Biedl syndrome not only has a melanophore-expanding action on frogs, but produces in the minnow (*Phoxinus laevis*) a reddish discoloration around the bases of the fins.

The sickly faecal smell of melaena is diagnostic, but rarely of importance; the same applies to the pungent smell of paraldehyde in the breath. It is alleged that there is a mouse-like odour in typhus fever, but I have not enough experience to know if this is so. It seems likely to me that as typhus thrives among dirt and poverty mice are likely to thrive in the same place, and so the smell of mice may be due to mice making a smell.

It is a common delusion among paranoid psychotics that a fearful odour emanates from their bodies. A foundryman attended my out-patient department complaining that a month previously a new and rare chemical was tried in the smelting process experimentally and that it had contaminated his blood so the fumes were still coming out all over his body. As I sat listening to him, tactfully angling for evidence of other delusions, the students behind me began to sniff restlessly, and I was uncomfortably conscious of an unpleasant, garlic-like smell which grew so strong the window had to be opened. His story was true in every particular. The chemical to which he had been exposed was tellurium, rarely used in the steel industry because of this distressing complication. If a minute amount of tellurium is absorbed, the body continues to excrete the noxious gas dimethyl telluride for many weeks afterwards.

With that account of an occasion when the sense of smell saved a man from possible certification, I bring to a conclusion my account of the use of the five perceptual senses in clinical medicine. Along these five routes comes the raw material which we fashion into clinical knowledge. We fashion it by means of the words we use in recording and describing it, and also by the thoughts, sensible or foolish, which we devote to its contemplation. The other two lectures deal with the sense of those words and the wisdom, or otherwise, of those thoughts.

Fig. 5 is reproduced by permission of Dr. C. J. C. Britton and J. and A. Churchill Ltd.

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The first international directory of medical equipment using radioisotope sources for treatment of malignant tumours has been issued by the International Atomic Energy Agency. The new publication gives all the necessary specifications of 46 models of teletherapy equipment produced by 18 manufacturers in Canada, France, Germany, Italy, Japan, Netherlands, Sweden, the United Kingdom, and the United States. The information is presented in such a manner as to enable the reader to make a quick reference to the main specifications of various units and to compare them and choose the most suitable one. The directory also contains a supply section in which prices of both teletherapy units and the radioisotope sources for such units and the names and addresses of the suppliers are given. The directory may be obtained in the United Kingdom from H.M.S.O., P.O. Box 569, London, S.E.1. (Price 12s.) *Radioisotope Teletherapy Equipment.* International Directory. International Atomic Energy Agency, Vienna, 1959.

INFECTION OF BURNS*

BY

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Compared with the specific fevers and with any infection that arises in healthy tissue, infection of burns presents a confused picture. This is due to various factors, the most obvious being our difficulty in telling which pathological changes are caused by infection and which are caused by the initial trauma itself. Confusion also arises from the fact that many burns heal well even when heavily colonized by bacteria; moreover, mixed rather than pure cultures are isolated from most burns, and for this reason it may be hard or impossible to recognize which bacteria are to blame for a manifest infection. While there is no dispute about the pathogenicity of *Streptococcus pyogenes*, other organisms—for example, *Pseudomonas pyocyanea* — have been regarded as pathogens of greater or less significance, dismissed as saprophytes, and sometimes even welcomed as allies against the more obvious enemy.

Clinical accounts of infection can be clearly recognized in the earlier literature on burns. Fabricius (1607) speaks of an *ulcus profundum et putridum* after the separation of burn slough; Dupuytren (1833) found abundant suppuration, fever, wasting, and death in patients with deep burns even when they were not extensive; and Bird (1855) said of the fever and inflammation in burned patients that they were not essentially different from such symptoms after other kinds of injury. Lister was aware of these infections, but unlike some of his contemporaries—for example, Pirrie (1867) and Maylard (1892)—he made no serious attempt to extend his antiseptic discipline to the treatment of burns—probably because the defence of burns against contamination was assumed to be an impossible objective (Lister, 1909; Dunbar, 1934).

Local and general injury by bacteria colonizing burns was recognized by various authors—for example, Lustgarten (1891) and Stockis (1903)—but the detailed study of burn flora was not undertaken until many years later. In 1926 Pack reported that practically every burn becomes contaminated within a few hours, the commonest organisms present being streptococci, staphylococci, and *Ps. pyocyanea*. These findings were extended by Aldrich (1933) and by Cruickshank (1935), who attributed the "toxaemia" and fever often found on the second and third days after burning injuries to septic infection of the burned surface. These authors and Wilson *et al.* (1938) emphasized the importance of streptococci; Marsh (1935) and Heggie and Heggie (1942) regarded *Staphylococcus aureus* as an important pathogen of burns. In the United States, Langohr *et al.* (1947), reporting a detailed bacteriological study of the burned surface, considered haemolytic streptococci and staphylococci particularly damaging to deep burns, the latter especially when present together with organisms of the *Proteus* group.

The work initiated by Colebrook in Glasgow (Colebrook *et al.*, 1944) and carried on by him and later by his collaborators at the Birmingham Accident Hospital has been concerned primarily with the protection of burns against infective organisms; it has been supported by studies on the epidemiology and chemotherapy of these infections, the pathogenicity of the bacteria, and the natural defences which the body puts up against them.

*Lecture given at the Postgraduate Medical School, Hammersmith Hospital, on May 6, 1959.

Bacterial Flora of Burns

Techniques

In our studies on hospital in-patients (between 300 and 400 a year) we have used swabs moistened with 10% broth in physiological saline for sampling the burn surface on admission, at every change of dressings, at operations, and daily if the burn is treated by the exposure method. The swabs are inoculated on horse-blood agar (containing 4 to 6% agar to prevent the swarming of proteus) and in cooked-meat broth, which is subcultured after overnight incubation at 37° C. to blood agar and to a selective medium for *Ps. pyocyanea* (Lowbury and Collins, 1955). All colony types are examined for morphology in Gram-stained films, and various confirmatory tests are made—a tube coagulase test for *Staph. aureus*, grouping of streptococci by Lancefield's method, examination for pigments of *Ps. pyocyanea* (Lowbury, 1951), urease tests for proteus (Cook, 1948), and, at certain times, biochemical tests for the classification of coliform bacilli (Report, 1956). For limited periods, too, we have examined burn swabs for the presence of *Clostridium welchii* and *Cl. tetani* (Lowbury and Lilly, 1958a, 1958b), and for anaerobic cocci by the method of Thomas and Hare (1954). Other examinations included in this study are the serological typing of many strains of *Str. pyogenes* and *Ps. pyocyanea*, phage-typing of *Staph. aureus*, and sensitivity tests by a ditch-plate method with appropriate antibiotics, especially for *Staph. aureus* and *Str. pyogenes*.

The patients are treated in two open wards, with limited cubicle isolation space in one of them. Burns which are treated by the "closed" method are dressed by a no-touch technique in a plenum-ventilated dressing-station (Bourdillon and Colebrook, 1946), supported by various other methods of combating cross-infection, including the oiling of floors and blankets (more recently the use of cotton cellular blankets) and isolation of patients with streptococcal infections (see Colebrook, 1950).

Observations

The bacteria which are isolated from burns by these methods vary with the time since injury, the area of the burn, the place where the patient is being treated, and the type of treatment given.

A typical bacteriological record of the burn of a patient during the period of hospital treatment is shown in Table I. The skin bacteria are killed at the time of burning, and swabs taken shortly afterwards are sterile or very sparsely contaminated. After 24 hours a variety of organisms will be found growing in all but the most superficial burns and in some of those—for example on hands and feet—which are protected by good cover (see example in Table II). During the first two to three weeks Gram-negative bacilli, including *Ps. pyocyanea* and proteus, are apt to predominate, accompanied by *Staph. aureus*, micrococci, *Str. faecalis*, diphtheroid bacilli, and aerobic spore-bearing bacilli in various combinations. *Str. pyogenes* is sometimes common, and at other times is absent from the wards for long periods. Anaerobic cocci are relatively rare and also tend to be absent for long periods. In the later

TABLE I.—*Bacteria Isolated from Burns (Example). Deep and Partial-thickness Burns of Hands and Face, both Legs, and Perineum; Estimated Area, 15% (Imperfect Cover)*

Burn Site	Bacteria on Burn	On Admission	During Weeks								
			1	2	3	4	5	6	7	8	9
Right thigh	Strep. Gp. A ..	0	0	0	0	0	0	0	0	0	0
	Staph. aureus ..	0	±	0	+++	+	+++	+++	++	+++	+++
	Ps. pyocyanea ..	0	0	+++	+++	±	++	±	±	±	±
	Coliforms	0	+++	0	±	+	+++	+++	+++	+	±
	Others	±	0	0	0	0	0	0	0	0	±
Local treatment		Dressings (penicillin cream)			↑ Operⁿ (85% take)	Dressings (tulle gras)			↑ Operⁿ (55% take)	↑ Exposed	

weeks after the separation of slough, *Staph. aureus* and (when it is about) *Str. pyogenes* tend to predominate in unhealed burns. Table III shows the time of the first appearance of various organisms in a series of burns; *Str. pyogenes* is conspicuous for its tendency to appear in the later stages, often in small unhealed areas.

The bacterial colonization of burns in hospital is an extreme example of what is generally called "hospital infection." The bacteria reflect the environment rather than the flora brought in by the patient on his skin and mucous membranes. Once or twice a year, for example, we have experienced an outbreak of infection with *Str. pyogenes*, which is often of one serological type. The staphylococci which we find in burns to-day (see Table IV) include a preponderance of strains belonging to phage group III and a fairly high proportion of group I (type 80) strains; from 80 to 100% are resistant to penicillin, and a large proportion are also resistant to the tetracyclines and to erythromycin. The Gram-negative bacilli are also different in various ways from the alimentary flora, and are clearly acquired by cross-infection; *Ps. pyocyanea*, for example, is very common in burns, especially if they are extensive, but it appears in only about 3% or less of normal stools (Sevitt, 1945; Lowbury and Fox, 1954). Strains of *Proteus* and of *Klebsiella* are also common in burns; faecal *Escherichia coli*, on the other hand, is at times among the less-frequent coliforms of the burn flora.

TABLE II.—*Bacteria Isolated from Burns (Example). Deep and Partial-thickness Burns of Both Legs; Estimated Area, 5% (Good Cover)*

Burn Site	Bacteria on Burn	On Admission	During Weeks					
			1	2	3	4	5	6
Left leg (below knee)	Strep. Gp. A ..	0	0	0	0	0	0	0
	Staph. aureus ..	0	0	0	0	0	±	0
	Ps. pyocyanea	0	0	0	0	0	0	0
	Coliforms ..	0	0	0	0	0	0	0
	Others ..	0	0	0	0	±	±	++
Local treatment		Dressings (penicillin cream)		↑ Operⁿ (95% take)		Dressings (tulle gras)	↑ Exposed	

TABLE III.—*First Appearance of Bacteria on Fresh Burns (5 Months)*

Organism	1st Week (%)	2nd Week (%)	3rd Week (%)	Later (%)	Total Infections
Str. pyogenes ..	21	25	4	50	24
Staph. aureus ..	76	18	2·5	3·5	115
Ps. pyocyanea ..	54	30	10	6	63
Proteus ..	38	36	19	7	74
Coliform bacilli	68	21	10	1	90

TABLE IV.—*Phage Groups of Staph. aureus in Birmingham Accident Hospital, 1957–8*

Phage Group	Casualty Department (Noses)		Burns Unit (Burns)	
	Penicillin-sensitive	Penicillin-resistant	Penicillin-sensitive	Penicillin-resistant
I (type 80) ..	7 (2)	1 (0)	2 (0)	23 (21)
II	12	3	0	0
III	13	3	7	54
Unclassified ..	1	0	0	2
Not typable ..	29	12	1	4
Total ..	62	19	10	83

The burned tissue forms a slough which usually separates in two to three weeks. While it occupies the site of injury, the slough is a hospitable medium for many bacteria, especially Gram-negative bacilli, where they can multiply relatively undisturbed by the natural defences and protected against antibiotics. After the slough has separated, the surface of the burn consists of granulation tissue on which *Str. pyogenes* and *Staph. aureus* flourish, but the Gram-negative bacilli, which grow less well in fresh serum, appear to be at a disadvantage; hence the preponderance of Gram-positive cocci at this stage.

The larger the area of the burn and the longer it remains unhealed, the greater is the likelihood of colonization by pathogenic organisms, such as *Ps. pyocyanea*, and also by relatively transient saprophytes, such as *Cl. welchii*. *Cl. tetani* was not found in a series of 273 swabs from burns, and there has been only one case of tetanus in an in-patient during the past 10 years.

Prophylaxis

Bacterial colonization may perhaps not interfere with healing of superficial burns, but it is desirable to prevent these from becoming a reservoir of pathogens which may infect patients in the ward with deeper burns. When the burns are of deep partial thickness and full skin thickness, prophylaxis is more directly important. For full-skin-thickness burns new skin is undoubtedly the best defence against infection (Ross, 1950), but infection, if it appears first, is one of the worst enemies of a new skin. For burns which cannot be excised and grafted on admission to hospital, therefore, other means of excluding bacteria are necessary.

Colebrook and his colleagues aimed to achieve not total asepsis but a selective shielding of burns from pathogens—and especially from *Str. pyogenes*—in the environment by the use, whenever possible, of ample dressings in layers of gauze, cotton-wool, and crêpe bandage. This physical barrier was supported by other

methods, and in particular the following: (1) a "no-touch" dressing technique (McKissock *et al.*, 1941; Williams *et al.*, 1944); (2) the use of a plenum-ventilated dressing-station; (3) the use of local prophylactic chemotherapy (with penicillin cream); and (4) chemotherapy and bed or cubicle isolation for known infections in the ward. The simultaneous application of these methods in Birmingham was associated with a lower incidence (5%) of streptococcal infection than was found in Glasgow (30%), where prophylactic penicillin cream and plenum ventilation were not used; there was, however, no obvious reduction in the incidence of infection by *Staph. aureus, Ps. pyocyanea,* and proteus (Colebrook *et al.*, 1948).

About 10 years ago we started a series of controlled trials to assess the relative merits of these and other techniques in protecting burns against colonization by pathogens. Patients eligible for inclusion in these trials were divided by random selection into two groups, one of which received the prophylactic treatment under investigation while the other was treated as a control series; details of treatment other than that under investigation were comparable in the two groups, and whenever possible the identity of the treatment and control groups was unknown to those who were treating the patients and analysing the results.

1. Chemoprophylactic Trials

Prophylaxis Against Str. pyogenes.—A trial of local penicillin prophylaxis was carried out on patients admitted to hospital with small or medium-sized burns which did not have immediate skin-grafting or require shock treatment (Jackson *et al.*, 1951a). Patients in the treatment group had their burns dressed on admission and at every change of dressings with penicillin cream (mostly 1,000 units/g.), or sprayed, if they were exposed, with a penicillin solution; the control burns were dressed with the cream base, or sprayed with distilled water. Analysis of the results (see Fig. 1) showed that 1.7% of 58 burns treated with local penicillin application picked up *Str. pyogenes,* as compared with 38% of 42 burns in the control group.

Prophylaxis Against Ps. pyocyanea.—Preliminary studies with polymyxin E showed that all strains of *Ps. pyocyanea* isolated in our unit were sensitive to the antibiotic, and appreciable increases in resistance did not occur on attempted habituation *in vitro* and during a prophylactic trial in burns (Jackson *et al.*, 1951b). This trial was carried out in the same way as the trial with penicillin, except that, in this one, both treatment and control creams contained penicillin (1,000 units/g.), the treatment cream containing, in addition, polymyxin E (1 mg./g.); solutions were used for spraying the exposed burns. The results of this trial are also presented in Fig. 1. Out of 160 burns treated with polymyxin and initially free from *Ps. pyocyanea* 11 (7%) became colonized by the organism, as compared with 50 out of 207 (24%) burns in the control series. There was a smaller but still significant difference in the proportions of added coliform bacilli in the two groups, but no difference in the proportions of *Str. pyogenes* or *Staph. aureus,* which are resistant to polymyxin.

Prophylaxis Against Staph. aureus.—The frequent carriage of *Staph. aureus* by normal subjects and the tendency of staphylococci to produce antibiotic-resistant variants frustrated our earlier attempts at

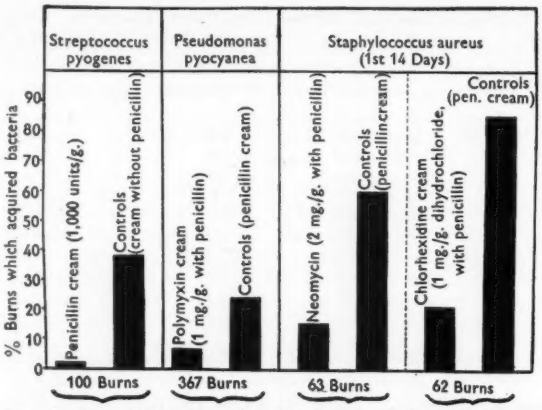

FIG. 1.—Bacteriological results of four controlled trials of local chemoprophylaxis directed against specific pathogens (see Jackson *et al.*, 1951a, 1951b; Lowbury, 1955).

prophylaxis against these organisms. Successful prophylaxis with chlortetracycline, for example, was demonstrated in controlled trials when the antibiotic was new, but was not maintained on account of the appearance of resistant staphylococci which became predominant in the burns unit after a few months (Lowbury *et al.*, 1952). On the other hand, the local application of neomycin, bacitracin, and chlorhexidine has not, in our experience, led to the emergence of resistant variants. Significant protection against added *Staph. aureus* (see Fig. 1) has been obtained in preliminary trials of local prophylaxis with creams containing neomycin (2 mg./g.) and chlorhexidine dihydrochloride (1 mg./g.) (Lowbury, 1955).

Combined Chemoprophylaxis.—In recent trials, which will be reported separately, the combined application of polymyxin, chlorhexidine, and neomycin has been found effective in prophylaxis; many burns remained apparently sterile, and added infection, with *Staph. aureus* in particular, was greatly reduced in the patients receiving this prophylactic cream.

2. Physical Methods of Prophylaxis

Plenum-ventilated Dressing-station

Bourdillon and Colebrook (1946) showed that the agitation of contaminated textiles—for example, removal of dressings—caused a build-up and a sustained high level of airborne bacteria, including wound pathogens, which could be prevented by plenum ventilation of the room. Using a plant that delivered 20 changes of filtered air per hour, they found that the numbers of airborne bacteria were negligible five minutes after the departure of a patient from the dressing-room. Another patient admitted at this stage could therefore be dressed in clean air.

In a controlled trial on patients with burns of small or moderate extent (Lowbury, 1954) it was shown that added infection of burns with *Ps. pyocyanea,* with antibiotic-resistant *Staph. aureus,* and with proteus was significantly lower in patients dressed in this room with the plenum plant working than in the control series whose dressings were changed by the same team in the same room, but without plenum ventilation (Fig. 2). Streptococcal infections were also consistently less common in patients dressed in the ventilated room, but coliform bacilli were evenly distributed in the two

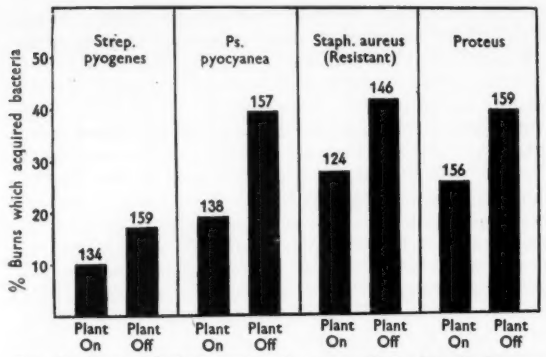

FIG. 2.—Bacteriological result of a controlled trial of plenum-ventilated dressing-station for burns (see Lowbury, 1954).

groups. As the patients spent a very small fraction of their hospital time in the dressing-station these differences are striking, especially in view of the opportunities for cross-infection that exist in the ward.

In a study on the serological types of *Ps. pyocyanea* (Lowbury and Fox, 1954) it was found that each ward had, for a time, its own predominant serotype of *Ps. pyocyanea* in spite of the shared dressing-room (Fig. 3). From this we may gather that cross-infection is also very common while the patient is lying in the ward. Air, floor dust, nurses' hands, and the bedding and bandages of patients are demonstrable reservoirs and vectors of these organisms. Burns treated by the exposure method or with imperfect cover are especially prone to contamination in the wards.

Exposure Treatment versus Dressings

It has been argued that a dry surface, such as that which forms over a burn exposed to the air, does not favour bacterial growth, and that the eschar protects the burn from contamination (Wallace, 1949; Blocker *et al.*, 1951; Körlof, 1956). There are clinical advantages in treating burns of the face and certain trunk burns by the exposure method, but burns in these areas are, in fact, more apt to be colonized by *Str. pyogenes*, *Ps. pyocyanea*, and other pathogens than burns of the hand and the foot, which can be satisfactorily covered with dressings (Table V). Moreover, the eschar, which often shows few bacteria on its outer surface, is apt to enclose a pool of pus (Lowbury *et al.*, 1954).

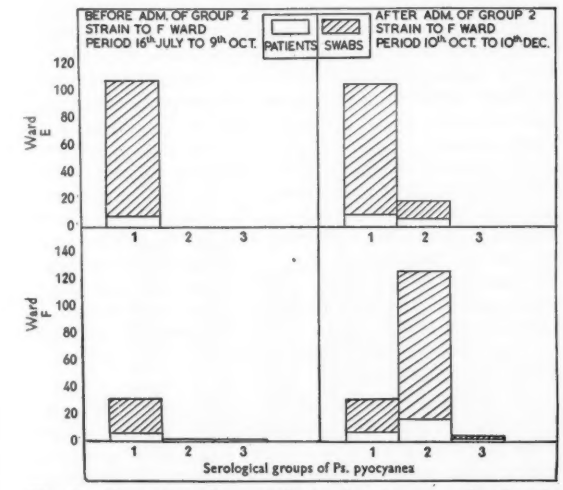
BEFORE ADM. OF GROUP 2 STRAIN TO F WARD PERIOD 16th JULY TO 9th OCT.
PATIENTS
SWABS
AFTER ADM. OF GROUP 2 STRAIN TO F WARD PERIOD 10th OCT. TO 10th DEC.
Ward E
Ward F
Serological groups of Ps. pyocyanea

FIG. 3.—Illustration of cross-infection in a burns ward: after the admission of a patient with *Ps. pyocyanea* of serological group 2 to Ward F, that organism became predominant in Ward F only, though two wards shared the same dressing-station and operating-theatre (see Lowbury and Fox, 1954).

The application of a cream under dressings facilitates the separation of slough and the use of local chemotherapy and prophylaxis; local prophylaxis with powder on exposed areas is clearly not very effective, for penicillin-lactose powder was insufflated on to all the face burns in our series, which, as I have said, acquired *Str. pyogenes* more often than any other sites. On the other hand, the application of cream and dressings encourages the growth of those bacteria which can reach the burn and which are not suppressed by the antibiotic barrier; for example, *Ps. pyocyanea* grows in dressings soaked with exudate and produces there large amounts of the blue pigment pyocyanin, a powerful toxin for skin cells (see below). This mechanism may perhaps account for the findings of Holman *et al.* (1956), who describe quicker healing of experimental burns in pigs treated by exposure than under dressings. The problems raised by these findings require further study. From the existing data it seems that each method has advantages which are determined by the position of the burn, the climate, the patient's preference, and various details of treatment.

TABLE V.—*Organisms Acquired by Burns on Different Parts of the Body (Admissions During 12 Months)*

Site of Burn	*Str. pyogenes* %+	*Staph. aureus* %+	*Ps. pyocyanea* %+	Coliform Bacilli %+
Face	13·9	93	38	55
Hands	6·1	55	20	27
Feet	1·6	48	15	41
Arms	9·9	83	48	63
Legs	10·1	73	52	62
Trunk	13·7	85	50	76
Total burns ..	732	571	691	650

Comments on Prophylaxis

Each of the prophylactic measures we have tested contributes only a partial protection of the burns, and the best results may be expected from their combined use, preferably with others that we have not had an opportunity of testing—for example, cubicle isolation of all or most of the patients.

Chemoprophylaxis can be successfully maintained only if the organisms against which it is directed do not acquire resistance to the agent applied to the burn. This requirement is met by penicillin against *Str. pyogenes*, by bacitracin and chlorhexidine against *Str. pyogenes* and *Staph. aureus*, by neomycin against *Staph. aureus*, and by polymyxin against *Ps. pyocyanea*. Unfortunately, antibiotics which might be used for the systemic prophylaxis of burned patients are, with the exception of penicillin, likely to induce the selection of resistant variants, and no satisfactory local or systemic chemoprophylaxis exists against proteus and some other groups of Gram-negative bacilli.

Pathogenicity of Burn Flora

Local Pathogenic Effects

Inflammation at the margins of the burn, lymphadenitis, and lymphangitis are sometimes present, especially when streptococci of group A are growing

in the burn; suppuration is very common, though not always easy to detect in exposed burns or to differentiate from residues of antibiotic cream in those treated with dressings. The most obvious criteria which can be measured are the results of skin-grafting operations and healing-times (cf. Bodenham, 1943; Clarkson and Lawrie, 1946). It is easy to show a direct association both of prolonged healing-time and of graft failure with higher frequency of *Str. pyogenes*, *Ps. pyocyanea*, and other organisms on burns of full skin thickness. Further evidence, however, is required before these bacteria can be stigmatized as the cause of such adverse effects, for it is certain that burns which take a longer time to heal also stand a greater chance of picking up these bacteria.

The evidence has come from trials in which bacteria have been excluded or eliminated from some of the burns by antibiotic therapy. In a trial of chlortetracycline for the treatment of *Str. pyogenes* infection, for example (Fig. 4), it was found that all but 2 out of 18 grafts "failed"—that is, showed less than 80% take—when the streptococcal infection was not adequately treated before operation, but only 11 out of 44 grafts failed when successful chemotherapy was used (Lowbury and Cason, 1954). In the controlled trial of polymyxin described above, grafting results were significantly better and the healing-time of burns of full skin thickness was significantly (on the average three weeks) shorter in the series protected with polymyxin (Fig. 5). Similarly, the use of successful chemotherapy or prophylaxis against *Staph. aureus* has been found to improve the results of skin-grafting (Lowbury, 1957).

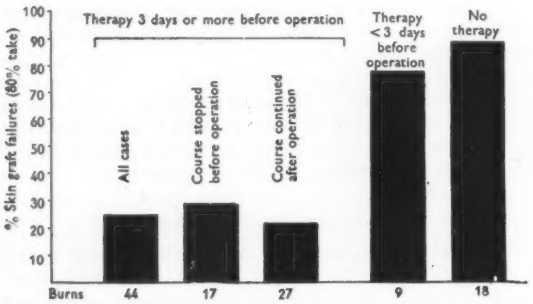
% Skin graft failures (80% take)
Therapy 3 days or more before operation
Therapy <3 days before operation
No therapy
All cases
Course stopped before operation
Course continued after operation
Burns 44 17 27 9 18

FIG. 4.—Effect of oral chlortetracycline against *Str. pyogenes* on the results of skin-grafting (see Lowbury and Cason, 1954).

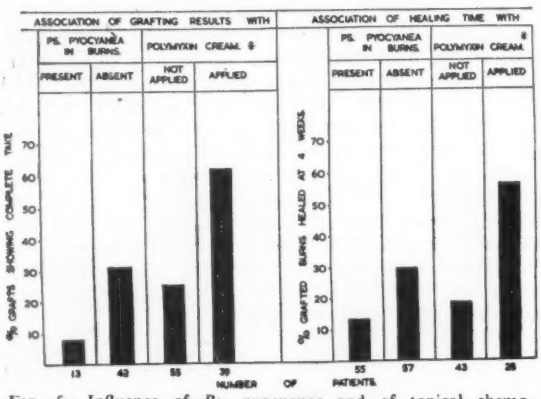

FIG. 5.—Influence of *Ps. pyocyanea* and of topical chemoprophylaxis on skin-grafting and on healing-time. When more than one grafting operation was required for any burn the worst result only is recorded in the assessment (see Jackson *et al.*, 1951b).

The mechanism by which bacteria cause these adverse local effects has received some attention. In the case of *Ps. pyocyanea* the pigment pyocyanin has been shown to cause necrosis and to inactivate respiration of human skin-tissue cultures in concentrations much lower than those which are estimated to be present in green burn exudate (Cruickshank and Lowbury, 1953; Lawrence, 1958). Staphylococcal α-toxin has been shown, by Dr. Lawrence in our unit, to have a similar effect on skin cells, but the toxin could not be detected in exudate on dressings over burns heavily colonized by *Staph. aureus* (Lawrence, 1959). How *Str. pyogenes* causes still greater damage to skin grafts has not been fully explored. Lawrence (1959) has shown that streptolysin O inhibits the respiration of skin cells. It has been suggested that streptokinase is of particular importance, as it is likely to prevent attachment of skin grafts to the receptor tissues: other factors, however, must also be involved, for streptococci of group C are often found in burns without causing graft failure, in spite of their production of abundant streptokinase.

General Pathogenic Effects

Str. pyogenes was formerly a common cause of septicaemia; Cruickshank (1935), for example, reported its isolation at necropsy from the spleen of three out of six patients with streptococci in their burns. The picture has changed since the introduction of the sulphonamides and penicillin. For many years we have not seen any cases of *Str. pyogenes* septicaemia in the Birmingham Burns Unit; other burn organisms, however, are often found (sometimes in enormous numbers) in the blood of severely burned patients. *Ps. pyocyanea* and *Staph. aureus* are probably the most dangerous and also the commonest invaders (Jackson *et al.*, 1951b; Liedberg *et al.*, 1954). Liedberg and his colleagues reported septicaemia in 15 out of 35 fatal cases of burns. Mixed infections are common. Markley *et al.* (1957), in Lima, found that *Ps. pyocyanea* septicaemia was a common cause of death in patients with extensive burns.

Str. pyogenes infection, even in quite small burns, is commonly associated with fever, sometimes after an apyrexial period—for example, Fig. 6. Pyrexia and hyperpyrexia in severely burned patients without demonstrable septicaemia may be due to bronchopneumonia or, more rarely, to meningitis or pyelonephritis; but the local infection of an extensive burn by Gram-negative bacilli, staphylococci, and other organisms can probably cause pyrexial reactions and contribute to the severe general illness of these patients. In the trial of prophylaxis by polymyxin there was a consistently lower frequency of pyrexia, anaemia, and death in those who received the prophylaxis than in the controls—presumably through the exclusion of *Ps. pyocyanea* and other polymyxin-sensitive organisms. The presence of Döhle bodies in the leucocytes of the more extensively burned patients (Weiner and Topley, 1955) may also, perhaps, be the result of infection.

Bull and Fisher (1954) found little improvement in the mortality results from burns after the period 1942–7 in spite of advances in treatment. In the later series, however, there was a longer period of survival of all but the most severely burned patients, and those who were saved during the shock phase were likely to die later from other complications. Of these, infection was the most important, and of the infective agents *Ps. pyocyanea*

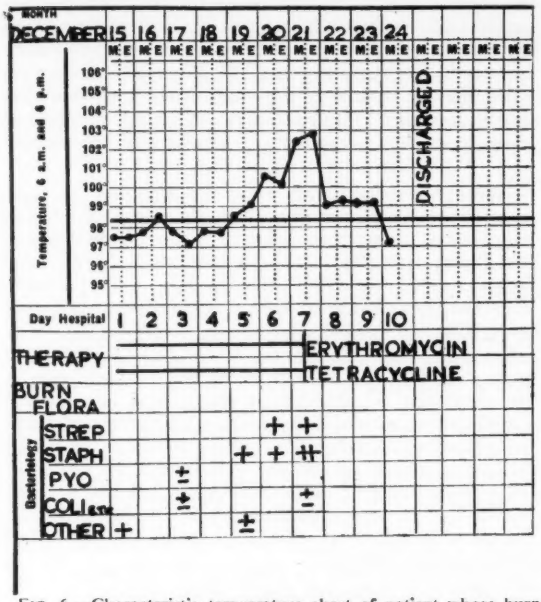
MONTH
DECEMBER
15 16 17 18 19 20 21 22 23 24
M E M E M E M E M E M E M E M E M E M E
Temperature, 6 a.m. and 6 p.m.
106° 105° 104° 103° 102° 101° 100° 99° 98° 97° 96° 95°
DISCHARGED
Day Hospital 1 2 3 4 5 6 7 8 9 10
THERAPY
ERYTHROMYCIN
TETRACYCLINE
BURN FLORA
Bacteriology
STREP
STAPH
PYO
COLI &c.
OTHER

FIG. 6.—Characteristic temperature chart of patient whose burn (of face only) became infected with *Str. pyogenes*.

has been most commonly associated with fatal septicaemia and bronchopneumonia in the same environment (Jackson *et al.*, 1951b).

Chemotherapy

Local Infections

By good fortune *Str. pyogenes*, the organism which causes the worst local effects, is the one most easily eliminated by chemotherapy (Fig. 7). Application of a cream containing 10,000 units of penicillin per gramme (Jackson *et al.*, 1951a) and of chloramphenicol (Liedberg *et al.*, 1955) have been found effective. Penicillin applied in lower concentrations or given systemically has in recent years proved unsuccessful in eliminating or even excluding *Str. pyogenes*, apparently because penicillinase-producing organisms are almost always

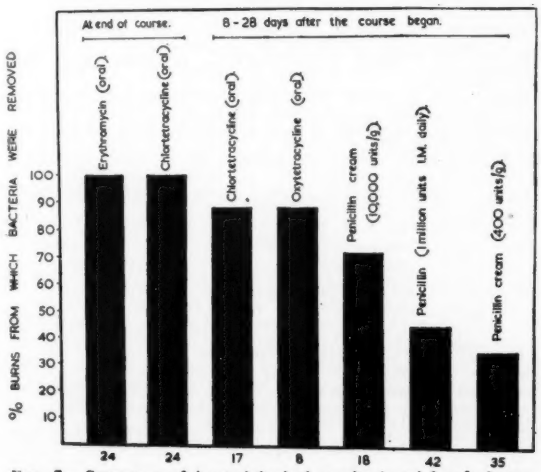
At end of course.
8-28 days after the course began.
% BURNS FROM WHICH BACTERIA WERE REMOVED
100 90 80 70 60 50 40 30 20 10
Erythromycin (oral)
Chlortetracycline (oral)
Chlortetracycline (oral)
Oxytetracycline (oral)
Penicillin cream (10,000 units/g.)
Penicillin (1 million units I.M. daily)
Penicillin cream (400 units/g.)
24 24 17 8 18 42 35

FIG. 7.—Summary of bacteriological results in trials of chemotherapy for infection by *Str. pyogenes* (see Jackson *et al.*, 1951a; Lowbury and Cason, 1954).

found in the same burns (Cruickshank *et al.*, 1948; Jackson *et al.*, 1951b; Körlof, 1954).

For this reason, and because *Str. pyogenes* appears most commonly in burns which are best treated without dressings, oral tetracycline and erythromycin have proved to be the most convenient antibiotics for the treatment of streptococcal infection of burns, which they will almost invariably clear of the streptococci in three days (Lowbury and Cason, 1954). Unfortunately, tetracycline-resistant streptococci of group A may emerge and become endemic in an environment where the drug is much used for the treatment of streptococcal infections (Lowbury, 1958). Erythromycin-resistance has also been encountered on a few occasions. For this reason it may be desirable to use the combination of erythromycin and tetracycline for hospital treatment of streptococcal burns.

Sensitive staphylococci can usually be eliminated from covered burns by combined therapy with novobiocin and erythromycin (Lowbury, 1957). Except when there is evidence of staphylococcal sepsis, however, the clinical advantage of removing staphylococci is probably outweighed by the risks of inducing the emergence of doubly resistant staphylococci; in burns treated by the exposure method this combined therapy is ineffective and resistance is especially prone to appear. Local application of chloramphenicol cream (10 mg./g.) has been shown to have some therapeutic value against *Staph. aureus*, and polymyxin cream (1 mg./g.) can sometimes clear *Ps. pyocyanea* from a burn (Jackson *et al.*, 1951b); these measures may be found useful in selected cases of clinical infection.

General Infection

Burn septicaemia is notoriously resistant to treatment. The organisms (especially the Gram-negative bacilli) are often resistant to most or all of the available antibiotics, but even when they are sensitive therapy commonly fails (Liedberg *et al.*, 1954). This is probably due to the fact that the burns are not cleared of the infective bacteria and the blood is continuously reinfected from this source. Staphylococcal suppurative thrombophlebitis has been successfully treated with chlortetracycline when the organisms were sensitive (Jackson, 1951). To-day the staphylococci that infect burns in hospital are usually resistant to the tetracyclines, and the readiness with which they acquire resistance to erythromycin and novobiocin makes these antibiotics uncertain therapeutic agents against staphylococcal infections of extensive burns. Fortunately, resistance of *Staph. aureus* to vancomycin has not been reported, and our initial experience of its use in staphylococcal septicaemia has been most promising (see also Davis *et al.*, 1958; Dutton and Elmes, 1959).

Natural Defences

Viable tissues have considerable powers of resistance against bacterial infection. Phagocytes, non-specific bactericidal agents, antibodies, complement, and other features of a "micro-environment inimical to the infectious agent" (Dubos, 1955) are recognized components of this defence mechanism. Meleney (1948) thought that serological immunity has little if any value in the protection of wounds against streptococci, staphylococci, proteus, *Ps. pyocyanea*, and other bacteria. Langhor *et al.* (1947), on the other hand, thought that an immune response to *Staph. aureus* contributed

towards the healing of burns. We found a raised serum agglutinin titre to the serotypes of *Ps. pyocyanea* in burns, the titre of agglutinins varying directly with the area of the burn and the duration of colonization with *Ps. pyocyanea* (Fox and Lowbury, 1953a). Rabbits immunized with these organisms gave smaller skin reactions on intradermal injection of the immunizing strains of *Ps. pyocyanea* than when *Ps. pyocyanea* of other serotypes were injected; there was evidence, too, of specific opsonizing activity by immune sera against the homologous *Ps. pyocyanea* (Fox and Lowbury, 1953b). Even if antibodies fail to remove bacteria from burns, they may perhaps have some value in preventing the organisms from spreading through intact tissue and invading the blood-stream. This view is supported by the association of septicaemia with reduced plasma gamma-globulin levels found in a recent trial (to be reported later).

There has been renewed interest in non-specific resistance in the past few years since the description by Pillemer *et al.* (1954) and Wardlaw and Pillemer (1956) of the properdin system. This bactericidal mechanism of normal serum operates in the presence of complement against a variety of organisms. *Staph. aureus* and *Str. pyogenes* are not sensitive to the properdin system; Gram-negative bacilli are often sensitive to it, but the types of Gram-negative bacilli commonly found in burns (*Ps. pyocyanea* and the *Proteus* and *Klebsiella* groups) are in our experience often resistant or slightly sensitive, in contrast with the intestinal *E. coli*, which are more often highly sensitive. Though properdin and complement titres are reduced in the serum of severely burned patients, the bactericidal activity of the serum against organisms sensitive to the properdin system is usually unaffected. It is clear that the value of this mechanism is very limited in the defence of the patient against the burn flora, though it may play some part in the selection of this flora (Lowbury and Ricketts, 1957; Willers, 1958).

The shortcomings of chemoprophylaxis and chemotherapy for infection of burns have prompted a renewal of interest in applying the principles of immunity. Rosenthal *et al.* (1957) have found that injection of gamma-globulin protects mice rendered highly susceptible to *Ps. pyocyanea* by burning or by cortisone. It is possible that the addition of gamma-globulin to the infusion fluid might help severely burned patients to resist invasion by an organism such as *Ps. pyocyanea* at the time when they are most susceptible to such infection.

Conclusions

Bacteria growing in deep burns can cause both local and general damage. *Str. pyogenes*, which has been reduced to negligible importance in other fields of surgery, is still the most formidable of the local burn pathogens, causing skin-graft failure, delayed healing, and deformity if it is not removed from the burn. *Ps. pyocyanea, Staph. aureus*, proteus, and other bacteria can sometimes also cause local damage, and are to-day more important as the cause of septicaemia and fatal infection than *Str. pyogenes*.

It has proved possible to keep a proportion of the burns free from *Str. pyogenes, Staph. aureus, Ps. pyocyanea*, and some of the coliform bacilli by a combination of physical and local chemotherapeutic barriers. Though the protection thus afforded is imperfect, it has proved clinically valuable. There is a dilemma involved in the choice between encouraging the formation of a dry adherent crust and using chemoprophylactic creams which keep the burn moist; when the former method is used, pathogens appear more frequently but perhaps cause less damage than they do when they can multiply not only in the burn but also in wet dressings. Future studies will include an attempt to combine the advantages of a relatively dry surface and of chemoprophylactic cover.

Another dilemma arises from the fact that the risks of infection are greater in burns units than when burned patients are nursed in general wards, though the facilities for expert treatment and research make burns units highly desirable in every other respect. It is probable that this dilemma can be solved by the development of units built and staffed with the aim of preventing cross-infection. The importance of protecting the burn surface from hospital flora must be emphasized, because the attempted prophylaxis of the patient by systemic antibiotics has proved disappointing, and routine therapy for established infection is impracticable or relatively ineffective except against *Str. pyogenes*.

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ACUTE ISCHAEMIA IN LIMB INJURIES

BY

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During the Korean war many injured limbs in which the main artery was damaged were restored to good function by the use of modern arterial techniques (Jahnke and Howard, 1953; Hughes, 1955). Correspondingly good results might be hoped for in comparable civilian injuries similarly treated. It is disappointing, therefore, that of nine such patients admitted recently to this unit attempts to save the injured limb failed in no fewer than six.

It is proposed to give a brief account of our experience, to study the causes of failure, and to make tentative recommendations for the management of such cases in the future.

Case 1

A 33-year-old man was admitted to hospital with a simple fracture of the left femoral shaft. It appears that at first the existence of circulatory impairment was missed and conservative treatment of the fracture was begun. Eight hours after admission it was realized that severe ischaemia was present in the distal part of the limb, and manipulation under anaesthesia was performed; the foot, however, remained cold and pulseless.

The patient was transferred to this unit and was operated on about 11 hours after injury. A 2-cm. segment of popliteal artery just below the adductor hiatus was found to be occluded completely by bruising and thrombosis. Resection of the segment with end-to-end anastomosis led to restoration of distal pulses. The fracture was fixed with a Küntscher nail. Next day there was gross swelling of the leg and foot, and fasciotomy was performed. The foot, though swollen, stayed warm and retained palpable pulses until the seventh day, when sudden complete ischaemia developed. Arteriography showed that the block was well below the popliteal bifurcation. Gangrene of the foot ensued, and below-knee amputation was performed on the fifteenth day. Though the posterior tibial artery was pulsatile at the level of amputation, the leg muscles showed extensive aseptic necrosis above this point. Convalescence was slow owing to delayed healing of the stump.

Comment.—Restoration of the circulation failed to reverse the damage done by more than 12 hours of ischaemia, so that extensive necrosis of muscle and late peripheral thrombosis ensued.

Case 2

A 56-year-old man caught his right arm in a moving belt, sustaining crushing in the elbow region, without fracture. He was seen soon afterwards in a local hospital, where occlusion of the brachial artery was diagnosed, and he was transferred without delay to this unit. Examination here showed that the elbow region was grossly bruised, the forearm and hand were white, pulseless, and numb, and contracture was present in the thenar muscles. At operation, six hours after injury, a 4-cm. segment of the brachial artery at the elbow was found to be occluded by bruising and thrombosis. The median nerve was anatomically intact. After excision and homograft replacement of the segment normal circulation was restored. Oedema of the forearm and hand ensued and persisted for several days. On recovery from the anaesthetic he was found to have a median-nerve palsy which took some months to resolve.

Comment.—Restoration of the circulation within eight hours was rewarded by the saving of a limb in which ischaemic contracture would have been inevitable and gangrene probable.

Case 3

An 82-year-old widow was admitted to hospital with a dislocated right shoulder. The right hand was ischaemic. The dislocation was reduced without anaesthesia, whereupon a large haematoma developed in the shoulder region. Thereafter the circulation in the hand was thought to have improved a little, though the radial pulse remained absent. Next day the ischaemic changes were more severe. The distal forearm and hand were pale, cold, and numb; the fingers were cyanotic, and severe contracture was present.

She was transferred to this unit 28 hours after admission, and was soon operated on. The axillary artery was found to be torn half-way across owing to avulsion of the posterior circumflex humeral branch, and was stretched over a large clotted haematoma. The involved segment was resected and a short homograft inserted. Good pulsation returned in the brachial artery down to the elbow, but the hand and distal half of the forearm remained ischaemic. Next morning arteriotomies were made at the wrist and at the elbow, and long string-like thrombi were washed out of the ulnar and radial arteries by the retrograde flush technique (Crawford and DeBakey, 1956). After this there was good circulation down to the wrist; the hand as far as the roots of the fingers was warm, but showed gross damage with vesication and discoloration; the fingers were gangrenous. The patient was treated conservatively with a view to limited amputation later. After about one week mental and physical deterioration started, and she died 15 days after the second operation.

Comment.—The circulation was reopened too late to prevent extensive ischaemic damage. Earlier repair of the artery might have saved the limb and the patient's life. In retrospect, amputation through the forearm should have been performed at the time of the first or second operation.

Case 4

A 21-year-old man was admitted to hospital with a compound fracture of the shaft of the right humerus. At operation extensive flaying of skin and crushing of muscle was noted, and the ulnar nerve was found to be severed. The brachial artery was thought to be in spasm, and attempts were made to restore circulation by applying papaverine to it. Next morning ischaemia of the hand remained complete, and there was severe contracture of the forearm muscles.

The patient was transferred to this unit and operated on approximately 12 hours after the accident. It was found

that a segment of the lower brachial artery close to the fracture was contused in appearance and diminished in calibre. An arteriotomy at this level revealed a small dark clot in the lumen, with a slender tail extending distally; when the clot was removed an area of lacerated intima could be seen. The contused segment was excised, the distal artery cleared of clot by retrograde irrigation, and direct end-to-end anastomosis performed. A good pulsatile circulation was restored to the limb, and this was followed almost immediately by a striking degree of oedema in the previously ischaemic area. Over the next few days massive oedema persisted; however, though sensation remained absent in the fingers, their temperature and colour progressively improved. By the fifteenth day oedema was less but had taken on a "boggy" quality; the patient had a high fever and looked ill. Surgical exploration showed massive liquid necrosis of the forearm muscles, and the arm was therefore amputated at the level of the fracture. Recovery was rapid. Dissection of the specimen showed that the arterial anastomosis and the arteriotomies were healthy and that the major arteries were free from clot.

Comment.—Restoration of the arterial supply was achieved after more than 12 hours' interruption. This failed in its purpose, however, because the forearm muscles had been irreversibly damaged by ischaemia. Indeed, though reopening the arterial flow had preserved the hand, it had probably converted what would have been a dry necrosis of the muscles into a moist gangrene.

Case 5

A man aged 28 was admitted to hospital with a dislocated knee, sustained as a result of a blow from a mechanical shovel. The dislocation was reduced, a haemarthrosis aspirated, and a plaster cast applied. At this time there was some anxiety about the distal circulation, but, as one observer thought he felt an ankle pulse, nothing was done other than to bivalve the plaster. Next day, about 18 hours after injury, the patient was transferred to this unit. At this time the foot was cold, blue, and numb, and there was marked contracture of the calf muscles. Exploration showed that the popliteal artery and vein were completely severed. The ends of the artery were trimmed and anastomosed, and the vein, which was full of clot, was ligated.

Post-operatively, massive oedema developed from the knee downwards, but there was good circulation, with a warm pink foot and palpable dorsalis pedis pulse. Oedema persisted, and during the second week became characteristically boggy. The patient became progressively more ill, with profound toxaemia and high fever. Several local collections of pus were drained, but it became clear that all the leg muscles were in a state of liquid necrosis. Above-knee amputation was necessary, and was followed by prompt recovery.

The dorsalis pedis pulse had been palpable throughout, and examination of the amputated limb showed the anastomosis to be healthy and patent.

Comment.—Re-establishment of the circulation after 18 hours' ischaemia averted gangrene of the foot, but amputation was necessary because of extensive necrosis of the calf muscle.

Case 6

An 8-year-old girl was admitted to hospital with a fractured left femur and an extensive flaying injury of the whole limb, sustained when she had been run over. After wound toilet and repositioning of skin, the fracture was reduced and a split plaster shell applied. On the fifth day after injury the foot was cold, blue, and numb, and there was marked contracture of the calf muscles. At this stage she was transferred to this unit, where arteriography was performed. This showed a patent popliteal artery and a slender circulation down the posterior tibial; the anterior tibial was not shown. It was decided that there was no indication for arterial exploration, but because of massive oedema a fasciotomy was carried out.

Over the next few days the foot became warm and pink except for the great toe; sensation did not return to the foot, and limited patchy skin-gangrene developed in the leg. High fever and toxaemia developed and the child became very ill.

Exploration of the calf showed gross liquid necrosis of muscle, but a strip of healthy muscle was present along the pulsatile posterior tibial artery. Since the foot was viable, consideration was given to excising the necrotic muscle; however, this was abandoned because of the extent of the damage and the severity of the toxaemia. Below-knee amputation was followed by rapid recovery. The child later walked well on an artificial limb.

Comment.—This case shows how severe ischaemia may result from injury to soft tissue even when the major arterial channels are open. This is an important factor, and is discussed more fully below.

Case 7

A youth of 18 had his ankle snared in a trawler's mooring hawser, sustaining a compression force presumably of many tons. He was admitted to hospital with a compound dislocation of the ankle. A good deal of skin remained intact, but most of the remaining soft tissues had been severed. An attempt was made to preserve the circulation by bridging the ends of the divided posterior tibial artery with a polyethylene tube. This soon thrombosed, however, and he was transferred to this unit. The polyethylene tube was replaced by a vein graft, but though the foot was perfused temporarily the flow soon stopped, probably for lack of sufficient venous return.

Below-knee amputation was performed a day or two later, and the patient recovered uneventfully.

Comment.—The original injury was virtually a traumatic amputation; after dissection of the specimen it was realized that the attempt at arterial repair had been hopeless from the first.

Case 8

A 26-year-old man fell through a glass roof, sustaining a large incised wound of the right arm and a closed injury of the left chest. The distal part of the right forearm and the hand were cold and pulseless, and there was anaesthesia of glove distribution. He had numerous rib fractures on the left side, with a limited area of paradoxical movement. He was admitted to this unit and operated on within five hours of injury. It was found that the brachial artery and the median nerve had been completely divided; the former was effectively sealed by its retraction within a sleeve of adventitia. The ulnar nerve had been nicked but not severed, and the biceps and brachialis had been extensively divided. An important feature was the venous damage; the cephalic and basilic veins and the brachial venae comitantes had all been cut. The artery was repaired by end-to-end anastomosis and primary suture carried out on the median and ulnar nerves. Full normal circulation was restored to the limb with no vascular sequelae. Sensation returned promptly, except for the expected area of median-nerve anaesthesia. Tracheostomy was required for the management of the chest injury, and thereafter the patient made a good recovery. At the time of writing the neurological deficit remained but the circulation was normal.

Comment.—The initial well-marked glove anaesthesia and its prompt relief by arterial repair indicate that the limb was saved from dangerous ischaemia by early operation. The absence of congestion after extensive venous damage is noteworthy, and supports

the belief that the oedema often seen after relief of ischaemia is not necessarily due to concomitant venous injury (see below).

Case 9

A 15-year-old boy was admitted to hospital with a closed fracture of the left femoral shaft at the junction of the middle and lower thirds. No significant circulatory impairment was evident until treatment by skin traction was begun; ischaemia then developed rapidly and progressed to stocking anaesthesia. On release of traction, adequate circulation returned to the foot, though ankle pulses were not restored. Any attempt to pull on the limb caused impairment of the circulation, and so traction was discontinued.

Next day he was transferred to this unit, where it was seen that there was no threat of gangrene, but that the fracture was in poor position. Exploration showed that a segment of lower femoral artery was looped round the bone end in such a way that traction on the limb caused complete obstruction. After the vessel was released there was good pulsatile flow in the involved segment, but pulsation did not extend further than the mid-popliteal region. On the suspicion that there was "consecutive" clot at this level, a popliteal arteriotomy was made. No clot was found, and there was no back-bleeding. However, after some external manipulation there was sudden profuse back-bleeding, probably from dislodgment of a fragment of clot. After repair of the arteriotomy good pulsation returned to the whole popliteal artery. Ankle pulses were still absent, but the circulation of the foot was so adequate that further procedures seemed unnecessary. The fracture was fixed with a Küntscher nail. Post-operatively there has been no anxiety about the condition of the foot. This was a recent case, and at the time of writing the patient was still under treatment for the fracture; the ankle pulses were then palpable.

Comment.—Prompt recognition of the ischaemia and its effective treatment by release of traction were the important measures in this case. Operation on the artery led to further improvement in the circulation and allowed the fracture to be treated.

Pathological Factors

The pathology of acute limb ischaemia has been reviewed by Scully and Hughes (1956) on the basis of experience in the Korean war. After a few hours' interruption of circulation a muscle contracture similar to rigor mortis develops. Scully and Hughes stress that this does not progress inevitably to fibrotic (Volkmann's) contracture, though the latter of course is a frequent sequel. In other words, this initial contracture, though of grave import, may be recoverable. These early changes may be accompanied by little or no histological alteration. Paradoxically, restoration of circulation at this stage often leads to sudden increase in the *apparent* severity of muscle damage. (It should be noted, however, that the previous "normal" histology may be merely that of dead or dying muscle preserved in a chilly environment). Thus there may ensue vascular engorgement, swelling, exudation, and focal haemorrhages, with release of myoglobin and consequent pallor of the muscles. The end-result may range from apparent normality, through varying degrees of patchy necrosis and regeneration, to complete death of the muscle.

These pathological changes correlate well with the clinical phenomena observed in this series and indeed in most cases in which acute limb ischaemia is relieved surgically—for example, embolectomy, or bypass-grafting for impending gangrene. Plethora and oedema of the limb develop, apparently in proportion to the severity of the preceding circulatory impairment. The changes may persist in diminishing form for months. Involved muscle may recover completely or may suffer any degree of damage (with subsequent fibrotic contracture) up to complete necrosis. Skin is more resistant to ischaemic damage than is muscle; unless the blockage is so peripheral that muscle largely escapes, the limb may be irretrievably damaged even though the skin remains viable (Cases 4, 5, and 6).

It is obvious, then, that acute complete limb ischaemia has a short time limit beyond which return of circulation is useless and may be dangerous; to restore blood-flow to the ischaemic area may rob the general circulation of much fluid by local extravasation and may release toxic materials into the blood-stream. Unfortunately the time limit cannot be defined categorically. Griffiths (1948) stated that "little good can come from attempts to relieve total ischaemia of 12 hours' standing." Our experience in the present series and in cases of embolectomy supports this conclusion, and suggests that even shorter periods may cause irreversible damage when the ischaemia is indeed total. However, since a trickle of blood may be reaching the periphery through collaterals, some latitude may be permitted short of endangering life from "tourniquet shock." We believe that this latter risk is small in healthy adults, but may be significant in the elderly, especially when circulation is restored to a large volume of ischaemic tissue. Though in some instances late restoration of blood flow may appear to precipitate a moist gangrene, this does not seem in our cases to have led to amputation at a higher level than would have been necessary in any event. Nevertheless, it is a possible danger that must be kept in mind.

Causes of Failure

There were only two causes of failure in this small series—extensive soft-tissue injury and undue delay in reopening an occluded main artery. The former may offer an insuperable barrier to recovery, but the latter should not.

The Factor of Soft-tissue Injury

Whenever the main artery to a limb is sacrificed, gangrene or residual disability is a significant risk, which varies with the level of arterial occlusion. Useful survival of the limb may be possible but cannot be relied upon, and at some levels—for example, the popliteal artery—the risk is critical (DeBakey and Simeone, 1946). The danger exists even with elective ligation; in traumatic cases it is increased by soft-tissue injury. For this, a number of factors are responsible. Thus there may be direct destruction of large areas of muscle, often with superadded infection. Widespread interruption of small vessels will affect the collateral circulation and can of itself cause ischaemia even though the main channels survive (Case 6). Finally, compression due to traumatic oedema may hamper the collateral circulation still further.

It follows, then, that if there is extensive soft-tissue trauma the effects of acute ischaemia are aggravated, and may in some cases become irreversible. Irreversibility should not be assumed too readily, however. The existence of soft-tissue injury should rather underline the urgent need for restoration of the circulation if the limb is to have the best chance of survival.

The high incidence of mangling and crushing injuries in our small series may have been an unfavourable

prognostic factor compared with other series, military and civilian, in which missile injuries and knife wounds predominate (Jahnke and Howard, 1953; Hughes, 1955; Morris, Creech, and DeBakey, 1957). However, the major cause of failure in our cases was delay.

The Factor of Delay

The situation in acute traumatic ischaemia is analogous to having a tourniquet on the limb. Treatment must be appropriately urgent.

As a technical procedure, restoration of blood-flow in the major arterial channels can be achieved even after considerable delay (Cases 1, 3, 4, and 5). The crux of the problem is that the circulation must be re-established during the all-too-brief period of viability of the ischaemic tissues, of which muscle is the most sensitive.

Some delay may be unavoidable if the patient's life is in danger from multiple injuries; resuscitation obviously takes priority over local treatment of the limb. In this respect restoration of a good general circulation by replacement of blood volume is of great importance; not only will the collateral circulation be benefited thereby, but the actual recognition of local ischaemia may be difficult or impossible during shock. *Avoidable* delay may occur in cases of established ischaemia for various reasons. Perhaps the commonest is what Griffiths (1948) aptly calls "an attitude of wishful thinking." It is compounded of the fear of doing harm by exploration and the hope that improvement may follow conservative treatment. Both the fear and the hope are misleading. In competent hands (and the number of surgeons with vascular experience is increasing rapidly) operation is unlikely to jeopardize the chances of survival of the limb; indeed, it may be wiser to explore than to observe the borderline case. The hope of spontaneous improvement, on the other hand, seems to rest principally upon two fallacies—that most major arteries can be interrupted with little risk to the limb, and that arterial spasm is a frequent cause of traumatic ischaemia. Of these two misconceptions the former has been discussed already. The latter, since it is of great importance, is considered here in detail.

We believe that there is erroneous emphasis on the role of "spasm" or "stupor" of the artery in the production of traumatic ischaemia. From experience with many different types of arterial case we feel that this has become a *mystique* which is to some extent based upon imprecise observation. A healthy artery is normally in a state of considerable elastic distension. When occluded, the vessel distal to the occlusion becomes narrow from elastic recoil, and this is often the basis for a diagnosis of spasm. For example, if after embolectomy the distal artery remains contracted and pulseless, it will be found to contain residual "consecutive" clot. Possibly this clot may induce some spasm of the artery containing it, but if the clot is removed completely by retrograde irrigation the "spasm" will disappear and pulsation return. Similarly, an injured arterial segment which is firm and pulseless almost invariably shows mechanical blockage from bruising, thrombosis, and interstitial haematoma, and the artery distal to this is contracted from loss of the *vis a tergo*.

It is significant that in a series of eight cases of supracondylar fracture of the humerus explored in the Mayo Clinic for ischaemia the artery was found to be completely torn across in two, thrombosed in two, stretched over the proximal fragment in two, pinched in a split in the bone in one, and impaled on a spicule in one (Lipscomb and Burleson, 1955). In other words, there was in every case a gross mechanical obstruction of the vessel. We do not deny the possible existence of arterial spasm as a cause of acute ischaemia, but feel that it would be wise to relegate it to a less prominent position than it holds in many authoritative writings. In this way waste of time in hopeful but futile spasmolytic treatment would be avoided.

Conclusions.

We believe that more of our patients could have been spared amputation (Cases 1, 4, and 5) and the one fatality avoided (Case 3) had arterial patency been restored in the first few hours after injury.

When the distal part of a recently injured limb is cold, pulseless, and of abnormal colour (pallid, cyanotic, or mottled), and especially if there is anaesthesia of the digits, then a dangerous degree of ischaemia exists. Unless simple measures (removal of splints, adjusting the position, for example, of the elbow) produce striking improvement within the hour, intervention as soon as possible is necessary. The presence of muscle contracture (rigor) calls for immediate exploration. Where possible the help of a surgeon specially experienced in vascular work should be obtained, but the procedures are within the compass of any general or orthopaedic surgeon who learns the simple basic techniques in anticipation of such an emergency.

In some equivocal closed injuries an arteriogram may prevent unnecessary exploration, but in most cases direct inspection of the artery at the likely site of damage is the most reliable course. At operation the lowest point of arterial pulsation should be defined. If the artery is found to be severed, the ends should be trimmed and anastomosed. Lateral tears are best treated by excision of the affected segment and anastomosis.

If "spasm" is found, the presence of clot is highly probable. The artery should be mobilized and occluded just above the lowest point of pulsation; gentle palpation then will often reveal the soft irregularity of clot in the lumen. The clot should be removed through an arteriotomy, and if inspection reveals intimal damage excision of the affected segment of artery is the wisest course. Direct anastomosis may be feasible after resection of segments up to about 4 cm. in length. If the gap is such that there is a risk of undue tension a reversed saphenous-vein graft should be inserted.

In every case, before the anastomosis is made, it is of great importance that all "consecutive" clot be removed from the distal artery. Normally there should be good back-bleeding from the distal stump. If there is any doubt about the patency of the vessel, it should be exposed at a lower level—for example, at the wrist or ankle—and flushed retrogradely, quite forcibly, with heparinized saline via a wide-bore needle or cannula. If this step has been omitted and if the arterial repair fails to restore distal circulation, this retrograde flushing should be performed through suitably placed arteriotomies.

In conclusion, we would emphasize that we do not advocate indiscriminate exploration of arteries on flimsy indications. On the other hand, we have attempted to

define certain rational grounds upon which operation should be undertaken urgently and resolutely.

Summary

Nine cases of acute traumatic limb ischaemia are presented. In spite of the fact that technically successful arterial repairs were performed in the majority, only three of the affected limbs were saved.

The pathology is reviewed and the causes of the failures are examined. Some are unavoidable because of associated soft-tissue injury, but the majority are attributable to simple delay in restoring blood-flow.

The reasons for this delay are discussed. It is felt that the aetiological role of arterial "spasm" in such cases has been overemphasized, to the detriment of their prompt and effective treatment.

A suggested scheme of management is outlined.

APPENDIX

Since submitting this article two further cases of acute ischaemia resulting from trauma have been encountered.

In one patient, a labourer aged 50, the axillary artery had been damaged by an injury to the shoulder. Operation was undertaken about four hours after the injury, and it was found that pulsation in the axillary artery extended down to a segment of narrowed contused artery beyond which the axillary artery was diminished in calibre and non-pulsatile. Exploration showed that continuity of the axillary artery was maintained only by a cuff of adventitia within which lay a thrombus effectively sealing the artery. The damaged portion was excised and the artery reconstructed by end-to-end anastomosis. An excellent result was obtained. In effect, the injury had completely severed the artery, and the ends were held in proximity by the adventitia; the outward appearances resembled some descriptions of "spasm" of the artery.

The other patient, a labourer aged 52, was first seen 14 hours after a severe crushing injury confined to the thigh. At this time there was complete ischaemia of the leg and foot with gross swelling and contracture of the leg muscles. At operation, traumatic thrombosis of the femoral artery at the adductor hiatus was found; the clot was removed from within the artery and a good popliteal flow restored. In view of the gross ischaemic damage to the leg, nothing further was done. Over the next 12 days the popliteal artery remained open, but massive septic necrosis of the leg muscles became apparent and the foot showed extensive gangrene, although two toes survived. A below-knee amputation was undertaken, during which a copious blood supply was encountered. In this patient the extensive injuries to the thigh had interfered with collateral circulation, so that occlusion of the main artery had caused almost complete ischaemia for 14 hours. Recognition of this ischaemia and relief by surgery within 6 hours of the injury might have saved the limb.

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INCIDENCE OF CHRONIC ARM OEDEMA AFTER TREATMENT FOR BREAST CANCER

BY

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Survival has long been the main criterion of success in cancer treatment. But morbidity should be considered as well as survival time. Five-year survival figures give no indication of the degree of discomfort that patients may suffer during that time. When some of this discomfort can be attributed to the method of treatment itself, full regard should be paid to this possibility when undertaking it. In this series of patients with breast cancer the morbidity due to swelling of the arm has been studied.

Arm-swelling is a common sequel to treatment for breast cancer and is often observed in the follow-up clinic, but the frequency with which it occurs has rarely been estimated with any accuracy. A wide range exists in the figures quoted for its incidence: from 8% (Aird, 1957) to 80% (Lobb and Harkins, 1949). This discrepancy is partly explained by different definitions of what represents a significant amount of arm-swelling.

Aird (1957) says that "arm-swelling is present to a considerable degree in only 8% of patients who survive five years." The definition of "a considerable degree" refers to Devenish and Jessop's (1937) study of 90 patients, of whom seven had sufficient swelling to "render the limb heavy and fatiguing to use, to cause disfigurement, to necessitate the wearing of special sleeves, and to produce undue susceptibility to inflammation."

Holman, McSwain, and Beal (1944) found that 44 out of 100 unselected patients had more than a 3-cm. increase in arm circumference measured 10 cm. above and below the olecranon process. Daland (1950) found than 22.5% had more than 2.5 cm. difference, but this group of 90 patients was selected more from his private than from his clinic practice. In Nicolson and Grady's (1948) review of 905 cases of carcinoma of the breast, 273 patients were surveyed for arm swelling and 36% had "slight," "moderate," or "severe" swelling.

The importance of arm-swelling as a symptom is rarely mentioned. Holman *et al.* (1944) give figures for "good," "fair," or "poor" arm function in relation to the degree of swelling. They point out that a significant degree of swelling may exist without recognition, unless measurements are made. On the other hand, when considering morbidity, the subjective aspect may be more important than the objective. Nevertheless, unnoticed arm-swelling, or swelling that is no inconvenience to the patient, may obviously be accepted in the treatment of breast cancer. Furthermore, subjective evidence is chiefly of individual significance and is not readily susceptible to statistical analysis. The subjective figures in this present series are of doubtful value, therefore, though it is important to consider subjective symptoms in a study of morbidity.

Method

To avoid any subsequent bias from taking the measurements, the subjective evidence was collected first. The patients were asked: "Is your arm swollen?" If they answered yes, they were then asked: "Does it bother you much, little, or not at all?" Patients would not always agree to this form of words, and often began complaining of discomfort in the axilla or shoulder, but it was usually possible to tie them down to an assessment of the arm-swelling itself in those words. They were also asked if they were left- or right-handed, since it seemed reasonable to suppose that the dominant arm might have a greater circumference than the other because of activity alone.

It was necessary to have a precise definition of arm-swelling. Probably the most accurate assessment is by measuring the volume of the arm by displacement of water (Stillwell and Redford, 1959). This is not practicable in a busy follow-up clinic, and so it was decided to measure the circumference of both arms above and below the elbow. Holman *et al.* (1944) measured at levels 10 cm. above and below the tip of the olecranon process, and this was repeated in the present series. They regarded a difference in circumference of more than 3 cm. as significant, but in this series 2.5 cm. was chosen because a short study of control patients and staff had shown none to have more than 2-cm. difference under normal circumstances.

Selection of Patients

Some of the figures given in earlier series were from selected patients while others were from comparatively small series. The object of this inquiry was to obtain reliable data by studying a large number of unselected patients. The follow-up clinic of the radiotherapy department in Oxford provided an opportunity for assessing the morbidity rate, since, with few exceptions, the general surgeons refer all patients with breast cancer to the department and these are all subsequently followed up. Usually the patients received post-operative radiotherapy, though a number had radiotherapy alone and a few were treated pre-operatively. It is reasonable to assume that almost every patient with breast cancer would attend the follow-up clinic in the course of a year's study. It is considered, therefore, that data on patients attending the follow-up clinic during one year would give reasonably accurate information on the true incidence of arm-swelling in the Oxford area.

The survey comprised 305 patients. This figure is lower than the total number of patients with breast cancer followed up in Oxford during one year, because of the exclusion of: (1) Oxford patients who had moved elsewhere and, though followed up, were not seen at our clinic; (2) patients who attended for follow-up but who had originally been treated at other centres, where surgical and radiotherapeutic techniques may have been different; (3) patients dying before coming into the inquiry; (4) patients failing to attend; and (5) patients with swelling due to cancerous invasion of the axilla. It is reasonable to claim that only in this last group was there any selection. Since the object of this survey was to study morbidity due to treatment rather than disease, this last group with neoplastic lymphoedema was necessarily excluded. The 305 patients thus form an unbiased sample.

Procedure

The study was conducted during the year from April 1, 1958, to March 31, 1959. The patients were seen at least nine months after the beginning of their first surgery or radiotherapy. This period was chosen to give time for all forms of treatment to be completed and for any temporary arm-swelling to subside (Parker, Russo, and Darrow, 1955). In addition to the subjective inquiry and arm measurements, the three classes of surgical treatment were distinguished (radical mastectomy, local mastectomy, or none); and the treatment or not of the axilla by radiation and the histological finding of axillary lymph-node involvement were noted.

Results

Of 305 patients measured, 109 (36%) were found to have 2.5 cm. or more difference between the circumferences of their arms. These measurements are analysed in Table I.

These numbers can be divided into two approximately equal groups: 58 patients with 2.5-5 cm. of swelling and 51 with more than 5 cm. This division has been used in Table II, where the data are analysed with respect to the various factors.

In Tables III and IV the subjective symptoms are considered.

TABLE I.—*Analysis of Measurements*

Diff. in circumference (cm.)	2·5–	5–	7·5–	10–	12·5–15	Total
No. of patients	58	29	13	7	2	109 (36%)

TABLE II.—*Analysis of Factors*

	Total No.	Cases of Arm-swelling		
		2·5–5 cm.	5+ cm.	Total
Nodes cancerous	135	38	30	68 (50%)
,, clear	135	19	19	38 (28%)
,, not examined ..	35	1	2	3 (8%)
Radiotherapy:				
Had treatment to axilla	211	50	46	96 (46%)
No ,, ,, ,,	94	8	5	13 (14%)
Surgery:				
Radical mastectomy ..	253	54	49	103 (41%)
Local ,, ..	41	4	1	5 (12%)
No operation	11	0	1	1 (9%)
Arm involved:				
Dominant side	139	30	24	54 (39%)
Other ,, ...	143	25	24	49 (34%)
Bilateral cancer	23	3	3	6 (26%)

TABLE III.—*Subjective Data*

	Possible Total	Actual No.
Correlation of subjective awareness with objective evidence of significant swelling	109	91 (83%)
Unaware of significant swelling	109	18 (17%)
Subjective symptoms, but no significant swelling ..	196	48 (24%)

TABLE IV.—*Subjective Symptoms Correlated With Amount of Swelling*

Symptoms	Measurements	
	2·5–5 cm.	5 cm. or More
Unnoticed	16	2
No trouble	20	11
Little ,, ...	21	26
Much ,, ...	1	12

Discussion

The 36% incidence of a defined degree of arm-swelling in an unselected series of patients treated for breast cancer approximates to a true morbidity rate, for the Oxford area at least. It is identical with the figure from Nicolson and Grady's (1948) comparable series of 276 patients. This shows that, with the present orthodox methods of treating breast cancer, one-third of the patients may expect a significant amount of arm-swelling afterwards.

Of the 109 patients with oedema, 60 (55%) complained of some inconvenience from this symptom, but most of these had only a little trouble. As might be expected, a greater amount of swelling was associated with more severe symptoms (Table IV). The subjective evidence is less reliable, of course, but there was a high positive correlation (83%) between the objective and subjective assessments. *Arm-swelling is thus a common symptom after treatment for breast cancer though it is often endured without great distress.*

Table II shows to what extent the incidence of arm-swelling is increased by the various factors: cancerous axillary lymph nodes (50% : 28%); radiotherapy to axilla (46% : 14%); and radical rather than local mastectomy (41% : 12%). It shows that it made no difference to the patient which arm was involved. (In fact, only five patients were left-handed, and two were ambidextrous, so that the dominant side was usually the right.)

Though it would be useful to be able to assess the individual contributions of these various factors, the percentages in Table II must be interpreted with care. This is because many of the patients received both radical surgery and radiotherapy for their breast cancer, and many of these will have had cancerous axillary lymph nodes. Thus all the three factors may be operating to a varying extent in the same patients, and these data can only provide relative figures for the influence of each. Even these may be misleading.

This point is illustrated by Table V, which shows how a more detailed analysis of the data may suggest different conclusions. After radical mastectomy and radiotherapy the incidence of arm swelling is seen to be identical, whether the axillary lymph nodes are found to be cancerous or not. After local mastectomy with radiotherapy the percentage is seen to be similar to the figure for those patients having no radiotherapy after their surgery. Some of these groups are small, however, and the figures may again be misleading.

Unfortunately it was not possible to analyse the severity of the radiation reaction at the axilla in these patients. At best this could only be done quantitatively, and in most of these patients the assessment would have been retrospective. But though they all receive the same nominal dose of *x*-rays, some patients suffer a more severe reaction in the axilla than others, and this may lead to a degree of fibrosis. Similarly some patients may have undergone a more "radical" radical mastectomy, which also may be followed by a tighter axillary scar. Here again only a qualitative assessment of the operation is possible, and this would require a surgical opinion, preferably by the same surgeon observing every case. It may well be that such a study of the severity of the *x*-ray reaction and the extent of the surgical dissection at the axilla, however qualitative, would provide the most important information about the aetiology of this arm-swelling.

TABLE V.—*Detailed Analysis*

			Total No.	Cases of Swelling
Received radiotherapy to axilla	Radical mastectomy	Nodes cancerous	132	67 (51%)
	"	clear	51	26 (51%)
	Local mastectomy	not examined	28	3 (11%)
	All cases with radiotherapy		211	96 (46%)
No radiotherapy to axilla			94	13 (14%)

Aetiology

In this series a significant degree of arm-swelling is attributable to the following factors: post-operative *x*-ray treatment to the axilla, cancerous involvement of the axillary lymph nodes removed at radical mastectomy, and radical mastectomy itself. (Swelling due to residual cancerous involvement of the axilla is another obvious factor, but the object of this study was to assess the morbidity of patients in whom there was no manifest involvement at the time of examination.) Unfortunately it was not possible to assess the contribution of post-operative infection and delayed healing in these patients, though the literature suggests that these are important factors.

It seems that *any* interference with the axilla (whether it be cancer, infection, surgery, or radiation) is likely to cause some disturbance of lymphatic and/or venous drainage in the axilla and that this is followed by swelling of the arm. Some of the previous literature on this subject is contradictory, however.

Veal (1937) classified post-radical mastectomy arm-swelling into three groups due to: (1) lymphatic obstruction, (2) constriction of the axillary vein, and (3) combined lymphatic and venous obstruction. Using venography, Veal (1938) found 90% of his cases were due primarily to venous obstruction. He made no lymphatic studies, however. Parker *et al.* (1955) found a direct relation between arm-swelling and increased venous pressure. They found that pressure increased immediately after operation and subsided in two to six months. On the assumption that this is a traumatic thrombophlebitis, they suggested "elastoplast" bandaging during this period and claimed that no patient had more than 2.5 cm. of swelling after this treatment. Again no lymphatic studies were made.

However, Devenish and Jessop (1941) found no evidence of venous obstruction in their cases. As well as measuring venous pressures they made lymphatic studies by dye injections, and concluded: "Lymphatic obstruction alone is sufficient to cause the swelling. Neither wound sepsis nor recurrent attacks of inflammation in the limb nor deep *x*-ray therapy is necessary for its development or persistence."

Nevertheless, post-operative infection and a severe radiation reaction in the axilla were factors in the series of 100 patients of Holman *et al.* (1944). Halsted (1921) also considered infection to be the main cause of "elephantiasis chirurgica," and he suggested a modified incision and skin-grafting in his radical mastectomy technique. Deaton and Bradshaw (1953) also suspected wound infection. But they found no relation between

arm-swelling and raised venous pressure, *x*-ray treatment, axillary metastases, arterial blood supply, or use of the arm. Wound infection and axillary scarring were the main factors in their opinion.

It is difficult to draw conclusions from this contradictory literature. But there seems to be no justification for denying that venous obstruction is a possible cause. This is not necessarily a direct result of axillary scarring, since Wyburn-Mason (1953) demonstrated the roles of costo-clavicular compression in four patients whose arm-swelling could be relieved by a sling support or excision of part of the first rib.

Post-operative and/or post-radiation scarring in the axilla is probably the most common factor, however, and the best conclusion from the present evidence is that of Aird (1955) that arm-swelling is "due either to the blockage of axillary lymphatics by malignant tissue, or to removal of the axillary lymphatic bottleneck in a radical amputation of the breast or to the fibrosis that follows high-dosage irradiation of the axilla."

Conclusion

This study has confirmed the clinical impression that arm-swelling often occurs after treatment for breast cancer. A morbidity rate of 36% can be expected when the method of treatment is radical mastectomy and post-operative radiotherapy, including the axilla. This is not to suggest replacing radical by local mastectomy, nor dispensing with *x*-ray treatment to the axilla. The survival rate is more important than the morbidity rate. But it might be rewarding to make a further study, as outlined above, to try to find out if a less radical mastectomy and a less severe axillary radiation reaction would be likely to reduce the morbidity due to arm-swelling without reducing the cancer survival rate.

Summary

Arm measurements were made of 305 unselected patients after routine treatment for breast cancer—a significant degree of arm-swelling was found in 36%. This morbidity rate is discussed.

Evidence was collected of the patient's subjective awareness of arm-swelling, and 55% complained of some inconvenience from this symptom. Significant swelling was found in 50% of patients whose axillary lymph nodes were involved with cancer, and in 28% of those which were not.

It was found in 46% of patients who had received *x*-ray treatment to the axilla and 14% who had not.

In 41% it was found after radical mastectomy, in 12% after local mastectomy.

There was no significant difference between left or right arm involvement.

The aetiology of arm-swelling is discussed.

I am grateful to the surgeons of the United Oxford Hospitals whose patients form the basis of this study. In particular, I thank Mr. A. Elliot-Smith, who has read this manuscript and made several helpful criticisms.

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"PREMATURE" CHILDREN AT PRIMARY SCHOOLS*

BY

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In an earlier paper (Douglas, 1956a) I described the mental test performances of 8-year-old children of low birth-weight. These "premature" children made consistently poor scores in both mental-ability and school-achievement tests when compared with a group of carefully matched controls. Their scores, unexpectedly, showed no clear relationship with either birth weight or length of gestation. Relatively high scores were made by those premature children born of mothers with a history of toxaemia or other abnormality during gestation, whereas the absence of such a history was associated with low scores. No adequate explanation could be given for these findings.

Further tests were given to the same groups of premature and control children when they were 11 years old, and the results of their 11+ secondary selection examinations are also known. In addition, their teachers have reported on their powers of concentration, discipline, and attitude to work. This new information is described in the present paper.

Background to this Study

A unique opportunity to make a controlled study of a representative group of premature children was provided by the Maternity Survey of 1946 (R.C.O.G. Survey, 1948). All children born during the first week of March of that year were enrolled in the inquiry, and among them were 706[1] legitimate single-born babies

*This inquiry is being made by a Joint Committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health, and the Population Investigation Committee. The chairman of the Committee is Professor James Young, the vice-chairman Professor A. Moncrieff, and the secretary Professor D. V. Glass. The Nuffield Foundation has taken a major part in financing this work and grants have also been made by the Board of Governors of the Hospital for Sick Children, Great Ormond Street (through the Institute of Child Health), by the Ford Foundation, by the Population Council (Inc.), and by the Medical Research Council. Fourteen regional hospital boards have also made grants to the inquiry from their free moneys.

[1] The number given in earlier papers was 707, but one child has since been excluded.

weighing 5½ lb. (2.5 kg.) or less at birth, and therefore, by international definition, "premature." Information was lacking on the home conditions of 31 of these premature children, but we have been able to match each of the remaining 675 with a child (the control) weighing more than 5½ lb. at birth who was selected from the remaining legitimate singletons (some 12,000 in number) born during the survey week. The selection was made on the basis of sex, ordinal position in the family, mother's age, social group, and degree of crowding in the home; and wherever possible the premature child was matched with a control living in the area of the same local authority.

Losses.—During the first 11 years of this study *unavoidable* losses through death and emigration have been heavy. In addition, as will be seen in Table I, a number of parents refused to co-operate, and some children were unable to take the tests owing to illness or mental backwardness. The greatest source of *avoidable* loss in the 11-year tests was late testing. The test booklets did not reach some schools until just before the holidays and were not completed until the beginning of the next term. This error of administration does not appear to have introduced a bias into the 11-year test scores, since the children excluded had 8-year test scores close to the average of the group from which they came.[2] As in previous papers, the absence of information on one member of a pair excluded the other member also from the analysis.

TABLE I.—*Losses from the Matched Sample (Birth to 11 Years)**

		8-Year Tests	11-Year Tests
Unavoidable losses	Death	178	179
	Emigration	36	39
Avoidable losses	Refusals	19	25
	Late or untraced	18	50
Inability to test	E.S.N. or M.D.	8	17
	Ill or physically handicapped	8	10
Completed all tests		408	355
	Total in sample	675	675

* These figures differ somewhat from those given in 1956. Owing to a clerical error some losses were attributed to emigration which should have been attributed to refusals or failure to trace. In addition, one child who completed only three out of four tests has been excluded from the analysis in this paper, whereas two other children whose test scores were not available in 1956 have been included.

Description of the Data Used

The tests used were designed for this inquiry by the National Foundation for Educational Research in England and Wales. They consisted of four tests given when the children were 8 years old and another four when they were 11 years 3 months. The tests given at 8 years were a picture intelligence test and reading, vocabulary, and sentence-completion tests. At 11 years the tests given were a mixed verbal and non-verbal intelligence test, and tests of reading, vocabulary, and arithmetic. The identical reading and vocabulary tests were used at each age. Both batteries of tests were given to the children by the primary-school teachers or, in a few instances, by educational psychologists.

The crude scores achieved by children in these tests have been converted into T scores based on all children at the particular age tested with a mean of 50, and a standard deviation of 10. This conversion was not used in the 1956 paper, and, as is shown below, has slightly altered the findings.

[2] The average test score at 8 years of premature children who were not tested at 11 years was 48.2 and the 8-year score of those tested in both years 48.0.

In addition to the two batteries of tests given by the teachers, the results of the 11+ secondary selection examinations were supplied by local education authorities. Children in Scotland were excluded from this part of the study because of the different method of secondary selection practised there, and a few children living in areas of England and Wales where 11+ examinations were not held were also excluded. Children going to private schools (10 premature and 19 controls) could not, of course, contribute to this part of the study, though they were included in the mental test studies, and we were left with 309 pairs, both members of which took the selection examination for local authority secondary schools in England and Wales.

Another view of the educational progress of these children was given by their teachers' comments on their attitude to work, powers of concentration, and discipline. These were made in response to questions put to the teachers when the children were 10 years old.

Lastly, special records of school absences were kept by the primary-school teachers.

Results

The main purpose of this paper is to describe the progress of premature children attending normal primary schools. In addition, six premature children and two controls were described as educationally subnormal or mentally defective at 8 years, and 11 premature children and six controls at 11 years.[3] The inclusion of these severely handicapped children, if we had been able to test them, would not have altered the picture given below, since they are few in number and are not confined to the premature group alone.

The test scores of the premature and control children are shown in Table II.

TABLE II.—*Test Scores in Tests of Mental Ability and School Achievement at 8 and 11 Years*

	Controls	Prematures	Difference
Tests at 8 years (408 pairs):			
Sentence completion	50·9	47·9	−3·0*
Reading	51·0	48·0	−3·0*
Vocabulary	50·0	48·3	−1·7*
Picture intelligence	50·5	47·7	−2·8*
Tests at 11 years (355 pairs):			
Reading	50·1	47·1	−3·0*
Vocabulary	50·3	47·3	−3·0*
Arithmetic	50·4	46·6	−3·8*
Mental ability	51·1	46·9	−4·2*

* Each of these differences is statistically highly significant when tested by Student's t-test.

The scores of the controls were consistently a little above the level to be expected—that is, 50—and the scores of the premature children consistently below it. The scores for the latter were lower at 11 years than at 8, whereas the control children made similar scores at each age. Thus, the premature children appear to become more handicapped as their age increases. They were similarly handicapped in all tests, and the suggestion made in 1956 that they were particularly backward in reading cannot be sustained now that test scores are used.

The premature children also did badly in the 11+ selection examinations. Only 9.7% gained a grammar-school place, as compared with 22.0% of their controls.[4]

[3] The figure of 11 premature children and six controls, who were reported as educationally subnormal or defective at 11 years, is a minimal one, since the comments of teachers show that some children, both premature and control, attending primary schools should in their opinion have been allocated to special schools.

[4] A highly significant difference.

TABLE III.—*Success in the 11+ Secondary Selection Examination Related to Mental Test Score*

11-Year* Test Score	Premature Children		Controls	
	G. S. Allocation %	Total in L. E. A. Schools	G. S. Allocation %	Total in L. E. A. Schools
<40	Nil	63	Nil	29
40–	Nil	46	Nil	51
45–	Nil	66	4·0	50
50–	1·9	54	12·5	72
55–	41·2	34	46·0	50
60+	70·6	17	73·2	41
Unknown	10·3	29	25·0	16
All children	9·7	309	22·0	309

* Average score on the four tests given at 11 years.

Within similar ranges of mental-test scores, however, the premature children were not at any substantial disadvantage (see Table III). The apparently better 11+ performance of the controls with test scores between 45 and 54 is based on only a few grammar-school places and is not statistically significant.

The results of the 11+ examination sometimes depend on the teachers' reports as well as on examinations and tests. It is therefore relevant to note that the teachers themselves made more adverse comments on the premature children than on their controls when asked to assess their powers of concentration, attitude to work, and discipline. Of the former 31% were the subject of one or more adverse comments as compared with 20% of the latter.[5] As with 11+ examination successes, the teachers' comments were closely related to the tested mental ability of the children (see Table IV).

TABLE IV.—*Teachers' Comments* Related to Mental Test Score*

11-Year Test Score	Premature Children		Controls	
	No Adverse Comment by Teacher %	No. of Children	No Adverse Comment by Teacher %	No. of Children
<40	36·7	79	34·4	32
40–	65·0	60	75·4	61
45–	71·3	87	74·3	70
50–	81·3	64	86·0	86
55–	89·6	48	90·2	61
60+	100·0	22	98·2	55
Unknown	72·4	29	75·0	24
All children	68·9	389	79·7	389

* Comments on attitude to work, power of concentration, and discipline.

To summarize, all four sources of information—mental tests at 8 and 11 years, the results of the 11+ selection examination, and the teachers' comments—show premature children as being considerably handicapped. The reason for this is discussed below.

Explanation of the Poor School Achievement of Premature Children

One possible explanation—that the premature children were more often ill and so missed school—may be immediately dismissed on the evidence of the school absence records. Between the age of 6 and 10 years they were away from school for an average of three weeks and one day per year whereas their controls were absent for exactly three weeks.

In an earlier paper (Douglas, 1956b) I was able to show that an apparent retardation in walking and talking among premature children was satisfactorily explained when their age was calculated from conception rather than from date of birth. But their poor performance in mental tests cannot be similarly explained, as will be seen from the following figures: children of birth weights of 5½ lb. (2.5 kg.) or less who were born within a week of term had an average 11-year test score of 46.9; those born one to four weeks early a score of 46.6; and those born *more* than four weeks early a score of 47.4.

It is unnecessary to discuss the relation between the level of test scores and the causes of premature birth, because the apparently poor performance of premature children in these tests is explained below in terms of the social and educational background of their families. As this survey progressed it became increasingly clear that, in spite of the careful matching of the premature and control pairs at the beginning of the survey for fathers' occupations, there were, in fact, marked social differences between them which have grown larger with time. The fathers of the premature children were more likely to move during the survey period to less favourable occupations than the fathers of the controls, and were less likely to improve their occupational status or move into self-employment. Moreover, periods of unemployment were more than twice as frequent among them—6.5% were unemployed on one or more occasions as compared with 3.2% of the fathers of the controls.[6]

As previously noted, even when drawing controls from a parent sample of more than 12,000 children, matches were not always satisfactory. But this does not explain either the difference in occupational history or the difference in test scores. The latter were just as great in the apparently "perfectly" matched pairs (283 in number) as in those less well matched. I therefore made a more detailed study of the social and educational background of the parents of these children, their standard of child care, and their interest in their children's educational progress.[7] The results are shown in Table V.

TABLE V.—*Comparison of the Social and Educational Background of the Parents and Standard of Maternal Care and Interest in School Progress*

	Families of		Difference
	Premature Children	Controls	
Social and Educational Background:			
% of grandfathers in non-manual work: Maternal	26·7	29·4	−2·7%
% of grandfathers in non-manual work: Paternal	27·6	36·9	−9·3%
% leaving school after the age of 15: Mothers	15·1	18·9	−3·8%
% leaving school after the age of 15: Fathers	14·7	17·3	−2·6%
% taking night classes or other courses after leaving school: Mothers	23·2	24·6	−1·4%
% taking night classes or other courses after leaving school: Fathers	17·6	24·7	−7·1%
Assessments of Maternal Care and Interest in School Progress:			
% rated favourably by health visitor in 1950 for: Management of child	33·7	45·1	−11·4%
% rated favourably by health visitor in 1950 for: Cleanliness of child and home	41·8	53·9	−12·1%
% rated favourably by teachers for interest in the child's progress at school	29·2	41·8	−12·6%

The social and educational background of both the mothers and the fathers of premature children was consistently less favourable than that of the controls. More of them came from manual workers' families, fewer stayed at school after the age of 15 or attended

[5] Another highly significant difference.

[6] A highly significant difference.

[7] Two assessments of maternal care were made by health visitors when these children were 4 years old. "Management" refers to sympathy and understanding of child; "cleanliness" to the care of clothes and shoes and to the cleanliness of the child and home.

night classes or other courses after leaving school. These differences were more pronounced for the fathers than for the mothers, and there is no suggestion here that the mothers of premature children have poorer social origins than their husbands.

According to the health visitors, the mothers of premature children showed poorer standards of both care and management, and according to the teachers they also showed less interest in their children's school progress. These three assessments of care and interest discriminated more sharply between the parents of premature and control children than did either the parents' social origins or standards of education. The relatively low proportion of premature children attending fee-paying schools (10% as compared with 19% of their controls) is a further reflection on both the economic circumstances of the families and the interest shown in education.

Preliminary tables showed that the test scores of premature children were particularly low when they came from a family that was less favourably assessed for social origins, education, or parental attitude than their controls, whereas when they came from a family more favourably assessed they scored as well as or better than their controls. For example, when premature children had parents whose educational interest was greater than the parents of their controls they scored 6% higher in the 11-year mental tests. When the interest of both sets of parents was the same they scored 5% less, and when the parents were less interested than the parents of the controls they scored 16% less.

In order to show more clearly the extent to which differences in parental background and attitude contributed to the poor achievement of the premature children, each pair was marked according to whether the premature child was superior to (+1), the same as (O), or inferior to (−1) the control on each of the following items: (*a*) social and educational background of both parents, (*b*) maternal care and management, and (*c*) interest in school progress. When the premature child was superior in all three a mark of +3 was recorded and when inferior in all three a mark of −3. A mark of O was given to those pairs where the premature child was assessed less favourably than the control for one item and more favourably for another as well as to those pairs where assessments were the same for all items.

These environment and interest marks show clearly the extent to which the premature children were drawn from less favourable family backgrounds than their controls—48% were rated unfavourably in these respects, whereas only 27% were rated favourably. The distribution of marks is given in Table VI.

Table VII shows the test scores and 11+ selection examination results after grouping the pairs in this way.

The premature children were consistently better than their controls when they were favourably assessed and worse than their controls when they were unfavourably assessed. But they were still at a slight disadvantage in both tests and in the 11+ examinations when they were assessed similarly to their controls—that is, had O marks.

Table VIII summarizes the progressive reduction in the handicaps of the premature children as their parents' social origins and educational aspirations get nearer to those of the parents of their controls.

TABLE VI.—*Distribution of Marks for Social Background, Maternal Care, and Interest in School Progress*

	+3	+2	+1	0	−1	−2	−3	No. of Pairs Full Information
Distribution of pairs (%)	4·9	8·0	13·6	25·4	21·9	17·9	8·3	374
	26·5% Premature children more favourably assessed.				48·1% Premature children less favourably assessed			

TABLE VIII.—*Test Scores (Average of Four Tests at 11 Years)*

	Premature Children	Controls	Difference	No. of Children
All pairs	47·0	50·5	−3·5*	354
Pairs with same interest in school progress	48·2	50·9	−2·7*	136
Pairs with similar assessment of social and educational origin, care, and interest (i.e., O marks)	47·6	49·3	−1·7	79

* A highly significant difference.

The same picture is found for the 8-year tests and the 11+ selection examination results, and it seems that if allowances could be made for all environmental differences the premature children would on the average do as well in these tests and in the 11+ selection examinations as their controls.

The position of very small premature children needs further mention.

Drillien (1958) reports that children of 3 lb. (1.4 kg.) or less in birth weight are likely to be grossly retarded at both pre-school and school ages. There are few children of really low birth weight in the present study,

TABLE VII.—*Scores and Grammar School Entry of Premature and Control Children Grouped According to Differences in Social and Education Background, Maternal Care, and Interest in School Progress*

Marks for Social and Educational Background, Maternal Care and Interest in School Progress	8-Year Tests			11-Year Tests			Grammar School Places*		
	T Scores		Difference	T Scores		Difference	Premature Children %	Control %	Differences %
	Premature Children	Controls		Premature Children	Control				
Favourable to premature child +3	54·9	48·0	+6·9†	53·2	47·2	+6·0	25·0	0·0	+25·0
Favourable to premature child +2	50·8	50·9	−0·1	51·0	50·6	+0·4	22·2	11·1	+11·1
Favourable to premature child +1	49·0	48·9	+0·1	48·3	48·9	−0·6	12·5	10·0	+ 2·5
Same 0	49·2	49·8	−0·6	47·6	49·3	−1·7	14·8	19·7	−4·9
Favourable to control child −1	48·2	52·2	−4·0†	46·6	52·2	−5·6†	5·7	28·3	−22·6†
Favourable to control child −2	46·8	52·8	−6·0†	45·6	52·3	−6·7†	6·1	32·7	−26·6†
Favourable to control child −3	44·1	54·4	−10·3†	43·8	55·8	−12·0†	0·0	47·6	−47·6†

* Excluding Scotland, areas in England and Wales where there was no 11+ allocation, and all children going to private schools.
† Highly significant.

but the matter is so important that the following figures —scanty though they are—may be of interest.

The relation of birth weight to 11-year-test scores was as follows:

	T score (average of four tests)
-4 lb. (1.8 kg.)	46.4
-4½ lb. (2 kg.)	47.5
-5 lb. (2.3 kg.)	46.4
-5½ lb. (2.5 kg.)	47.5

There were 41 survey children of birth weight 4 lb. (1.8 kg.) or less alive at 8 years. Three of these had gone abroad with their families, 35 were tested at either 8 or 11 years or both, and three were not tested at all for various reasons. The distribution of test scores is shown in Table IX, using 11-year average scores where available or otherwise the 8-year scores:

TABLE IX

Birth Weight	Test Scores (Average of Four Tests at 11 Years)				
	<30	30–39	40–49	50–59	60 and Over
3 lb. (1·4 kg.) or less	0	1	2*	1	0
-3½ lb. (1·6 kg.)	0	2*	4	3	0
-4 lb. (1·8 kg.)	1	7†	6	7	1

* One had 8-year test scores only.
† Two had 8-year test scores only.

Since there is a medical examination for the families of emigrants it may be accepted that the three children going abroad were not grossly defective and there is no evidence in their early histories to the contrary. [The birth weights of these children were 3 lb., 3 lb. 7 oz., and 4 lb.—(1.4, 1.6, and 1.8 kg.).]

The remaining three children were not tested, for the following reasons: 1 (birth weight 4 lb.: 1.8 kg.) E.S.N. attending a special school; 1 (birth weight 3 lb. 3 oz.: 1.44 kg.) now at a secondary modern school, normal early milestones—parents withdrew from survey when he was 4 years old; 1 (birth weight 4 lb.: 1.8 kg.) followed up until 6 years of age. No suggestion of retardation in medical examination by school doctor. Parents are separated and child may have been adopted.

These figures provide no evidence to suggest that these small babies form a special group which is grossly retarded in later life.

In 1946 there was a lack of special facilities for the care of small premature babies, and only the hardiest were likely to survive. It may be that as facilities have improved so have the number of survivors with mental handicaps. The improvement in national survival figures in recent years for babies of low birth weight is small, but in the Simpson Maternity Hospital, Edinburgh, which was the source of Drillien's cases, there appears to have been a substantial increase in the chances of survival of children in the smallest birth-weight groups.

Discussion

The additional material set out in this paper confirms an earlier study which showed that children weighing 5½ lb. (2.5 kg.) or less at birth make low scores in tests of mental ability and school achievement. It further shows that they are rated adversely by their teachers for attitude to work, power of concentration, and discipline in class, and that they fare badly in the 11+ secondary selection examinations. These handicaps, however, are to be attributed to adverse home conditions—in particular to lack of parental care and low educational aspirations—rather than to the effects of low birth weight or cerebral damage associated with it. The problem then reflects the complex social causes of prematurity. It has long been recognized that a high incidence of premature births is associated with failure to use the available antenatal services; it is also associated with poor standards of maternal care and lack of interest in educational progress.

There are compelling reasons for using controls when investigating a relatively rare condition such as prematurity. The cost and labour of observing a whole population in order to obtain information about a small section of it are prohibitive, especially when a longitudinal study is planned. Yet randomly chosen controls are likely to yield misleading comparisons if they differ in social and biological characteristics from the group under study, and we can seldom exclude this possibility.

In choosing controls for the premature children in this study I was in the fortunate position of being able to match for the characteristics that seemed at that time to be of major importance.[8] Unfortunately, as it turns out, they were not the only ones that mattered where educational progress was concerned, and a blind reliance on the method of paired controls would have led to a misleading interpretation of the differences observed. This was realized only after looking at information on social origins, educational background, and parental attitudes that had been collected for the purposes of an entirely separate study of social class and educational opportunity, and *not* for the purposes of the premature study. In other words, if this inquiry had been limited to a study of the mental development of premature children, the information required for a meaningful interpretation of the results would not have been available and incorrect conclusions would have been drawn. This raises a number of interesting questions about the advisability of using controlled comparisons in socio-medical studies. In particular, the fact that a control group is satisfactory at the beginning of a longitudinal inquiry does not mean that it will still be so at the end.

Summary

In a national study of the mental ability and primary-school progress of "premature" children a number of striking handicaps were found, which were later shown to be of environmental origin rather than the result of low birth weight *per se*. The preliminary findings were that premature children: (*a*) made consistently lower scores than their matched controls in eight tests of mental ability and school achievement (four given at 8 years and four at 11 years); (*b*) were the subject of more adverse comment than their controls by their teachers in respect of their attitude to work, power of concentration, and discipline in class; (*c*) were less than half as likely as their controls to gain grammar-school places in the 11+ selection examination.

These differences are largely explained by the fact that premature birth is not only associated with poor living conditions but also, at each social level, with low standards of maternal care and lack of educational interest.

This study casts doubt on the utility of the method of controlled comparisons in socio-medical studies.

I thank the chairman and members of the joint committee for their help and advice; the medical officers of health

[8] The alternative of selecting controls at random could hardly be considered owing to the excess of males, first-born children, etc., among the premature group.

and the health visitors whose generous co-operation made the survey possible; and the mothers in all parts of the country who willingly answered numerous and detailed questions on their children's health. I owe a particular debt of gratitude to Miss Patricia Heneghan, my research assistant.

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SARCOMATOUS CHANGE IN THREE BROTHERS WITH DIAPHYSIAL ACLASIS

BY

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Sarcomatous change is a rare but well-recognized complication of diaphysial aclasis which has never been recorded in two members of the same family. In the family described here, three affected brothers have died of bone sarcomas in the past 25 years.

"Diaphysial aclasis" (Keith, 1920) is the name commonly used on this side of the Atlantic, but there are several synonyms. Ehrenfried (1915) used the term "multiple cartilaginous exostoses," which has become recognized in the United States of America. Jaffe (1943) and Monro and Golding (1951) called the condition "hereditary multiple exostoses." "Multiple exostoses" was used by Abernethy (1830), Virchow (1876), and MacCallum (1940).

Two abnormalities of bone growth characterize diaphysial aclasis. There are osteochondromas, which are more numerous near the epiphyses of the long bones, which grow most actively (Fairbank, 1949, 1951). However, they have been described on all bones, including those of the face and skull, which are preformed in membrane (Honeij, 1920). The exostoses lie between the bone and the periosteum, and show no tendency to erode the parent bone. The ossification of the epiphysial plates of affected bones is disordered. Instead of the normal "row formation" of the epiphysial cells (Dodds, 1930; Johnston and Whillis, 1938), there are masses of cartilage of unusual thickness and patches of ossification. The general appearance is of uncontrolled cartilaginous growth, but without proper preparation for the deposition of cancellous bone. The affected bones fail to grow to their proper length, and the metaphyses are expanded into an irregular cylindrical shape.

The exostoses vary in number from one to 1,000. They appear at any time in childhood or adolescence, and continue to grow until bone-growth ceases at about the age of 20 years. After this they remain static unless malignant change occurs. By the age of 10 years 90% of exostoses have been discovered (Stocks and Barrington, 1925). The unequal shortening of the long bones of the legs causes an affected person to be below average height and to have abnormalities of stance such as kyphoscoliosis, coxa vara, knock-knees, and flat-feet. In middle age severe osteoarthritic changes are frequent in the weight-bearing joints. Bessel Hagen (1891) described the shortening of the distal end of the ulna with a tendency to dislocation of the wrist, which is said to occur in a third of affected people.

Family History

Eight members of this family have lived in Hoddesdon (Numbers 2, 3, 4, 7, 14, 15, 16, 17), and most of their relatives live in the Mons areas of Belgium. I was able to interview 21 blood relatives, and all except two of them allowed me to make a full clinical examination. The oldest living relative (Case 1) denied all knowledge of the family complaint, but she allowed me to palpate her arms and legs. I found exostoses around her knee-joints and osteoarthritic changes in these joints. Five of her seven children had diaphysial aclasis, and three of them have died from bone sarcomas. From the family tree (see next page) it appears that the common female ancestor, who is marked "R," must have carried the gene for diaphysial aclasis. Thirty-two of her direct descendants have been traced; 19 were examined fully; two were interviewed; seven were not seen personally; and four were dead at the time of this survey.

In this family there were seven affected males and six affected females. Ten females and nine males were not affected, but it is likely that some of the younger children will develop exostoses as they grow up. Adults with a very small number of exostoses may have been overlooked, as it was not possible to arrange for *x*-ray films to be taken of all members of the family.

All the affected persons had an affected parent. There was no instance of diaphysial aclasis being inherited through an unaffected parent of either sex. The 13 affected people have had a total of six affected male and four affected female children, as well as five unaffected children of each sex. Exactly half the children of the affected parents have diaphysial aclasis.

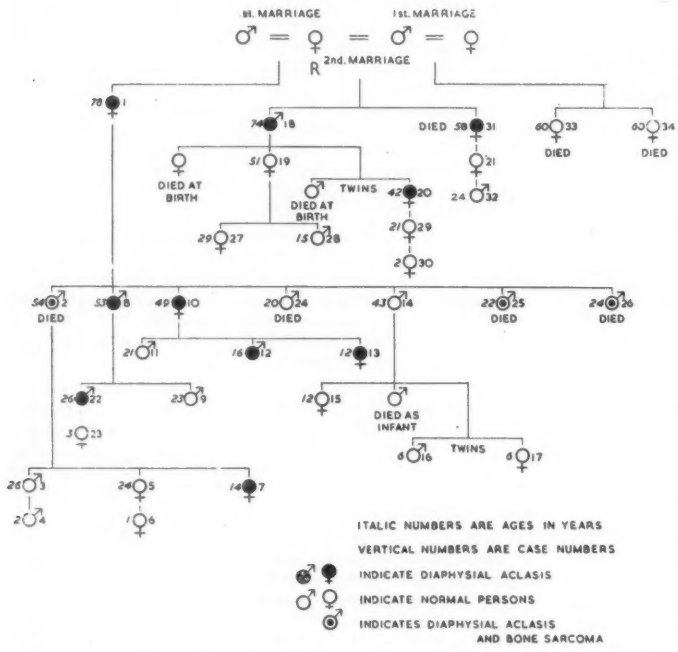
It was the "lumps on the bones" which the patients had noticed, and about which they talked. On the whole they had caused very little inconvenience. Only in Case 8 had an exostosis been removed from the lower end of his right radius, at the age of 11 years. The patient's right wrist had been weak since the operation as there was shortening of his radius, which may have been due to damage to the growing epiphysis. In no case was there any symptom from pressure of a benign exostosis on to a joint, tendon, artery, vein, nerve, pelvic outlet, or any other structure. In the nine cases examined the number of exostoses varied from 8 to 78, and were found on most of the bone that had been preformed in cartilage. No exostosis was found on a "membrane-bone." Exostoses were found around the knee-joints of all affected persons. Where an exostosis could be palpated it was usual for *x*-ray examination to reveal several other small nodules. In Case 7, who was 14 years old, the exostoses on her scapulae appeared larger by palpation than on the *x*-ray film. In this case the bulk of the exostoses must have been composed of radiolucent cartilage.

None of the patients had noticed the abnormal bone formation at the metaphyses. The cylindrical section and the abnormal internal structure of the affected metaphyses were easily seen on the *x*-ray films. None of the affected people were above average height, and in four cases (Nos. 2, 7, 10, and 12) one leg was 1 in. (2.5 cm.) or more shorter than the other. In four (Cases 1, 10, 18, and 20) out of seven of the affected people over the age of 40 osteoarthritis of the knees was very troublesome. Case 20 had well-marked coxa vara, knock-knees, and flat-feet, but these may have been due to healed rickets as she had been born near Mons in 1915, and had spent her childhood in this war-stricken area.

Case Histories

Case 2.—In 1956 this man died of chondrosarcoma of the ilium at the age of 54. He had always been aware of

numerous bony nodules on his body, but they had not altered since he was 20. At 42 and 46 years he had become worried lest the nodules on his femora were growing. *X*-ray films at these times confirmed the presence of numerous exostoses, but there was no evidence of malignant change. When he was 51 his wife noticed a new lump in his left buttock. It was the size of a hen's egg. There was no pain or tenderness in the lump, but his left leg ached slightly. Biopsy confirmed the clinical diagnosis of chondrosarcoma. Two full courses of radiotherapy were given. There was no dramatic tumour response, but it was thought that the lump grew more slowly for a time after this treatment. During the remaining three and a half years of his life he needed two chordotomies for the relief of intractable bone-pain, and a cystostomy because of acute retention of urine from an incoordinated bladder. The tumour of his left ilium grew to be 6 in. (15 cm.) in diameter. Anteriorly it pressed upon the abdominal and pelvic organs and posteriorly it ulcerated through the skin to become a necrotic mass. At the time of death there was no evidence of any secondaries, though a post-mortem examination was not allowed.



Case 25.—In 1936 this man died of a sarcoma of his "shin" at the age of 22. His close relations agreed that he had always had numerous bony tumours, but had enjoyed good health. Three years before his death one of the exostoses on his shin began to grow fairly rapidly. The affected leg was amputated and the family were told that he had a sarcoma. He died soon after this operation. No medical notes are available about this case.

Case 26.—This man was 24 when he died of a sarcoma of his pelvic bone in 1946. His close relatives agreed that he had several bony tumours, but he was accepted for the Belgian Army. He was well until nine months before his death. He was treated at the Institut Jules Bordet in Brussels in 1945, and a summary of his case notes is available. He complained of increasing constipation, which necessitated a colostomy. This was due to a bony tumour of his pelvis, which was diagnosed on radiological evidence as an osteosarcoma. No curative therapy was attempted, but a cordotomy was done to relieve his severe bone-pain. There are no records of necropsy, nor of a biopsy of his tumour. There was no evidence of metastases.

Sarcomatous Change in Diaphysial Aclasis

There is a specimen of a chondrosarcoma arising in an exostosis on the crest of the ilium in the Museum of the Royal College of Surgeons of England. Twenty-five other cases have been recorded in the literature, but in no family has there been more than one case. Single cases have been recorded by Weber (1866), Barlow (1895), Fennel (1938), Bennet and Berkheimer (1941), Ellis and Taylor (1951), Monro and Golding (1951), and Gros *et al.* (1957). Phemister (1930), Gardner (1937), and Geschickter and Copeland (1949) each reported two cases. Jaffe (1943) and Drevon *et al.* (1950) each reported three cases of chondrosarcoma complicating diaphysial aclasis. Stocks and Barrington (1925) found records of six instances of malignant change in 1,172 collected case histories.

Chondrosarcomatous change should be suspected in any exostosis that shows renewed growth at any time after the age of 20. In many cases it is difficult to confirm the diagnosis without biopsy. Several *x*-ray films taken at intervals of a few months show an expanding radiolucent tumour with patchy secondary calcification, which lies between the bone and the periosteum, and may erode both these structures. Microscopically it is possible to find areas containing many atypical cartilage cells in which double nuclei are common, though mitotic figures are unusual. There is a reduced proportion of cartilaginous matrix (Thomson and Turner-Warwick, 1955). In many cases, where tumours have been clinically malignant, pathologists have not found it easy to confirm the diagnosis microscopically (Platt, 1931; Warren, 1931). The diagnosis of chondrosarcoma was not included in the "Register of Bone Sarcomata" of the American College of Surgeons until after 1930.

Thomson and Turner-Warwick (1955) found a 50% 10-year survival in unselected collected cases of chondrosarcoma. It is a slow-growing tumour, which metastasizes to the lungs after many years. In Cases 2 and 26 there was no evidence of metastases. As in Case 2, the tumours are radio-resistant, and the only hope of cure is by amputation, which may have to include half the pelvis or the shoulder girdle.

Summary

A family which shows the typical features of diaphysial aclasis is described. In this family three affected brothers have died of bone sarcomas, but in only one of them was a biopsy available. The literature has been reviewed and reports of 26 other cases of chondrosarcoma complicating diaphysial aclasis were found. In none of these families did more than one member show this complication.

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SIGMOID VOLVULUS IN AN AFRICAN POPULATION

BY

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Volvulus of the sigmoid colon is an uncommon surgical emergency in the United Kingdom, and this point has been emphasized by Bolt (1956), who records only five personal cases and 23 others collected from the West Middlesex Hospital, the Bristol Royal Infirmary, and Weston-super-Mare General Hospital between 1946 and 1955. Vick (1932), reporting nearly 7,000 cases of intestinal obstruction occurring in 21 English hospitals between 1925 and 1932, found only 56 cases of sigmoid volvulus. Similarly, in the United States Hilton and Waugh (1951), from the Mayo Clinic, could find only 16 cases treated there during a period of 39 years. On the other hand, other American authors who have included cases occurring among negroes have significantly higher figures (Griffin *et al.*, 1945; Pool and Dunavant, 1951).

In Eastern and Northern Europe, however, volvulus of either large or small bowel is more common. Perlmann (1925) writes of 35 cases of sigmoid volvulus in a series of 200 cases of intestinal obstruction. Bruusgaard (1947) discusses 91 cases treated in one Scandinavian hospital over a period of 10 years. In India, Andersen (1956) found 24 cases among 168 of intestinal obstruction.

This paper describes the experience of sigmoid volvulus gained at Mulago Hospital, the teaching hospital of the University College of East Africa. This is a 628-bed general hospital which provides an emergency service for the African people of Kampala and the surrounding agricultural district, numbering about one million.

From a study of the literature it appears that no other hospital has the opportunity of dealing with such large numbers of patients presenting with sigmoid volvulus.

Incidence

That the incidence of sigmoid volvulus was high has been known at Mulago for a long time. Burkitt (1952) drew attention to this fact, and pointed out that its occurrence was almost entirely confined to one tribe.

The 104 cases of sigmoid volvulus under review were admitted to hospital during the five-year period 1952–6. Only cases proved either at operation or by post-mortem examination are included in this series. A further 18 cases of intestinal obstruction which are thought clinically to have had a sigmoid volvulus were excluded. These cases resolved either spontaneously or after a diagnostic enema.

Table I shows the numbers of cases of volvulus and intestinal obstruction treated during the five-year period. Table II gives the incidence of sigmoid volvulus among cases of volvulus and cases of intestinal obstruction. For comparison both Tables include Vick's (1932) findings in England.

TABLE I.—*Figures From Mulago Over a Five-year Period and From 21 English Hospitals Over a Six-year Period*

	Mulago	England
Sigmoid volvulus	104	56
Volvulus of transverse colon	2	0
,, ,, caecum	6	35
,, ,, small bowel	21	85
Total volvulus at all sites	133	176
Intestinal obstruction (excluding ext. herniae)	287	3,625
,, ,, (including ,, ,,)	1,230	6,892

TABLE II.—*Sigmoid Volvulus*

	Mulago	England	Rough Ratio Mulago/England
Percentage of all volvulus	78·2	31·8	2·5: 1
,, ,, intestinal obstruction (incl. ext. herniae)	8·45	0·81	10: 1
Percentage of intestinal obstruction (excl. ext. herniae)	38·1	1·45	25: 1

Table II shows that sigmoid volvulus forms 78.2% of all cases of volvulus, whereas in England cases in this category account for only 31.8%. Even more striking is the relation of sigmoid volvulus to the total number of cases of intestinal obstruction—ten times as many cases occurring. If external herniae, which also have an abnormally high incidence, are excluded, an even more marked difference is observed, the ratio between Mulago and English figures being roughly 25:1.

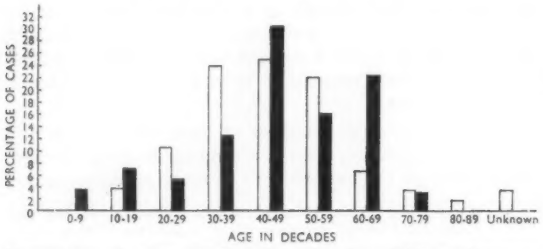
Double Volvulus. — Twenty cases of "double volvulus" are included among the figures for sigmoid volvulus. This is a clinical entity which does not seem to occur with sufficient frequency outside Buganda to have gained much attention. The double volvulus recognized at Mulago is a compound volvulus of the small bowel and sigmoid colon.

Sex and Tribe.—From Table III it can be seen that males formed 94.2% of the patients. This high figure

TABLE III.—*Incidence of Sigmoid Volvulus in Relation to Sex and Tribe*

	Male	Female
Baganda	80 (93%)	6
Other tribes	18 (100%)	0
Totals	98 (94·2%)	6

is in keeping with the findings of others, Peterson (1934) quoting 86%, Perlmann (1925) 85.7%, and Bruusgaard (1947) 61%, and is probably not just a reflection of the preponderance of male admissions generally. It can also be seen that the condition is four times more common among the Baganda than among other tribes. This figure is significant, as only 40% of surgical patients are Baganda tribesmen. Also the East African Population Census (1948) showed that in the three counties surrounding the hospital the Baganda formed only 53% of the population. Of the 66 male cases reaching hospital from this area 54 (81.1%) were Baganda.



Percentages of cases distributed in decades. White columns = present series. Black columns = Vick's (1932) English cases.

Age.—The Chart shows the age distribution of the cases, with Vick's English figures included for comparison. Most cases fall between the ages of 30 and 60. It must be admitted that the ages recorded may often be estimated on the part of the patient or clerk documenting the case. However, the errors will probably fall among patients in these decades rather than among the young or old, whose ages can more easily be judged. If these figures are accepted, it can be said that volvulus is not a disease of early life, and that, despite a fairly short expectation of life, the incidence in later decades is considerable. Except in regard to their shorter expectation of life, the age incidence among the African patients does not differ significantly from that of the English. It may be inferred that at least some factor in the causation of the condition is acquired.

Clinical Picture

The patient is commonly a well-nourished male Muganda between 30 and 50 years of age, giving a history of sudden onset of colicky abdominal pain around the umbilicus. The condition has been present from one to four days. Vomiting is usually associated with the onset of pain, but perhaps does not occur again unless the gut becomes gangrenous. Distension is marked and often gross enough to embarrass respiration.

Constipation is complete, and the patient states emphatically that neither faeces nor flatus has been passed, though a bowel movement is often mentioned as precipitating the attack.

A previous history of attacks of abdominal pain and mild distension, often associated with the taking of a meal, is commonly part of the picture. This is thought to be a consequence of the action of the gastro-colic reflex on a loaded pelvic colon which perhaps already has in it the 180 degrees "physiological twist" described by Bruusgard (1947). A history of previous frank attacks with either spontaneous resolution or relief by enemata is common.

On examination the patient's condition is found to be good and he is well hydrated, having continued to take fluids after the onset of pain. Distension of the abdomen is found to be gross and asymmetrical, being maximal in the right hypochondrium. Peristalsis is not usually visible, but gut sounds can be heard on auscultation. Tenderness is not marked or localized. The rectum is empty and ballooned.

When gangrenous gut is present, however, the general condition rapidly deteriorates, and all the features of severe peritonitis are found.

Operative Procedure

The patient is prepared for operation, and an intravenous infusion is set up as a routine. If shock occurs the use of whole blood is important because of loss of blood into the bowel wall and lumen of a strangulated loop.

A general anaesthetic is given, and a flatus tube is passed into the rectum before the operation is begun. If the diagnosis is reasonably certain a left paramedian incision is used, extending from the costal margin to the pubis dividing the thinned-out rectus muscle in the line of its fibres. An immensely dilated loop of bowel immediately presents and obscures the field of operation. If there is any difficulty in delivering the bowel it is emptied of its gaseous contents by needle aspiration. This procedure is certainly indicated where distension is gross, as there is a very real danger of rupturing the bowel after the support of the abdominal wall has been removed. The direction of the volvulus is now ascertained and the loop of the bowel gently untwisted. It is not until then that the flatus tube, manipulated per rectum by an assistant, is guided into the sigmoid by the hand of the surgeon. The contents of gas and liquid stool are evacuated.

At this point some important features of the macroscopic pathology of the disease can be noted. The sigmoid can easily be delivered out of the wound, and the whole colon and caecum are found extremely mobile on the posterior abdominal wall. The taenia coli of the sigmoid are found before deflation to be very broad, the individual fibres being apparently widely separated. After deflation the bowel wall is felt on palpation to be abnormally thick and tough in texture.

The redundant bowel is suspended from a long narrow mesocolon, and its proximal and distal attachments to the posterior abdominal wall are abnormally close together. The mesocolon is thick and oedematous and almost invariably shows signs of fibrosis, ranging from fine white strands to coarse fibrous bands approximating the limbs of the loop. In this thickened mesocolon the inferior mesenteric artery may be found, not running through it at its attachment but arched up towards the gut between its layers. From here the subsequent operative procedure depends upon the state of viability of the bowel.

In most cases there is no doubt about viability, but on occasion small areas, usually at the site of torsion, require to be oversewn. There may of course be obvious gangrene of the whole loop. If the bowel is to be preserved the mesocolon is shortened and fixed to the left paracolic gutter and the lateral and anterior abdominal wall by means of interrupted cotton sutures. If the bowel is gangrenous resection and the formation of a colostomy is carried out.

In performing the resection great care must be taken to divide the bowel from the mesocolon towards the

periphery, thus avoiding damage to the inferior mesenteric artery or its lower sigmoid branches.

Difficulty is often encountered in delivering the distal stump of the sigmoid colon, gangrene having extended near to its junction with the rectum. If this is the case the end is closed and buried in the posterior abdominal wall and a single-barrelled colostomy is formed (Gabriel *et al.*, 1953). This may be done either through the laparotomy wound or, better, through a left gridiron incision. Intraperitoneal closure of the colostomy is eventually necessary.

The wound is now closed and the patient returned to the ward with a flatus tube still in the rectum. Gastric suction and intravenous infusion of fluids are continued until bowel sounds are heard and flatus is passed.

A period of passive distension of the large bowel tends to follow reduction, and it is thought that this is due to a temporary paralysis of the gut musculature after extreme distension. It can be relieved by a flatus tube. The possibility of a recurrence of the volvulus must be borne in mind, however.

Mortality

There were 21 deaths among 104 cases, eight of these being among the 20 cases of double volvulus. The overall mortality rate is therefore 20.2%. If cases of double volvulus are excluded the mortality is 15.5%.

The length of history prior to admission seems to have no direct relation to mortality, as the average for those who survived was 2.3 days (83 cases) and 2.2 days for those who died (21 cases).

15 of the deaths were associated with gangrenous bowel, eight of them also having a double volvulus. The history of those with double volvulus was on an average less than one day, that for the remaining cases being 2.9 days.

Of the six fatal cases in which the bowel was viable, two patients died probably after a second volvulus, one collapsed on the operating table, one died with a wrong diagnosis of tuberculous peritonitis, one sustained a perforation of the small bowel during laparotomy, and one died for no known cause five days after operation.

Operative versus Conservative Treatment

The treatment of choice at Mulago has been operative over the period under discussion. There is, however, a good case put forward for more conservative treatment, and this was admirably done by Bruusgaard (1947). He reported a series of 91 patients who were treated conservatively where possible. The method was to intubate the sigmoid under direct vision through a proctoscope. At Mulago this method is not in regular use, but a short trial of the procedure in earlier years showed that a case with apparently viable bowel at the site of torsion may proceed to gangrene despite relief of the volvulus. The possibility of the presence of a double volvulus, which is very difficult to reduce even at laparotomy, is another contraindication to the use of this procedure.

No attempt at preventing a recurrence of the volvulus can be made unless a laparotomy is performed. In this series a primary attempt to obtain a permanent cure was made in 68 cases. This excludes those cases in which resection of gangrenous bowel was a curative procedure in itself.

The method which has become standard is to shorten and fix the mesosigmoid to the left paracolic gutter and the lateral and anterior abdominal walls with interrupted sutures of cotton. This procedure has the effect of turning what was a short anchorage into one having the shape of a T with an exaggerated down-stroke. It is thought that this is a logical method of overcoming the predisposing anatomical feature of a long mesocolon having a short base.

The emphasis is on a primary attempt at repair for the good reason that few patients will agree to a second operation once the acute phase has passed.

Aetiology

The aetiology of this condition remains a subject for discussion. The criteria that seem to be necessary for the production of a volvulus are that the sigmoid colon should be long and mobile, and that the points of attachment of its limbs should be approximated.

At Mulago many patients presenting with acute symptoms have a previous history of attacks of intestinal obstruction ; others with similar histories attend for treatment after the last incident has resolved. The latter group, together with those patients already mentioned who have a less well defined dyspeptic syndrome, consistently show at exploratory laparotomy one or both of the criteria suggested.

There is evidence that diet and feeding habits may also have a place in the aetiology of this condition. High-residue diets were incriminated by Bruusgaard (1947) and Andersen (1956). That of the Baganda, who eat large quantities of plantain and sweet potatoes, also falls into this category.

Summary

In the five-year period 1952–6 104 cases of sigmoid volvulus were admitted to Mulago Hospital, which serves the African population of Kampala and district. Sigmoid volvulus formed 80% of all cases of volvulus treated, and nearly 10% of the cases of intestinal obstruction. 94% of the patients were males, and the condition was four times more common among the Baganda than among other tribes. The operative procedure carried out at Mulago Hospital is described. The overall mortality in this series was 20%. The advantages of operative over conservative treatment are outlined, with particular reference to prevention of recurrences.

I owe a great debt to the surgeons of Mulago Hospital, whose cases I have been allowed to use. I also acknowledge the assistance I have received in the preparation of this paper from Professor I. W. J. McAdam, Professor of Surgery, Makerere College Medical School. Finally, I thank the Director of Medical Services for his permission to publish this article.

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UNSUSPECTED OESOPHAGEAL LEIOMYOMA FOUND AT HIATAL HERNIORRHAPHY

REPORT OF TWO CASES

BY

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Leiomyomas of the oesophagus are relatively rare. The chance finding, in seven months, of two leiomyomas during transthoracic repair of two apparently simple sliding hiatal hernias emphasizes again that hiatal hernias do sometimes occur in association with tumours in the lower third of the oesophagus, that some of these tumours may be undetectable despite barium studies and oesophagoscopy until operation, and that only by the transthoracic route can they be readily detected and treated.

Case 1

A farmer aged 56 was admitted to hospital on May 27, 1957. He gave a four-year history of epigastric discomfort, flatulence, dyspnoea, and hiccups which first began with heavy lifting when making concrete paths. His chief disability was severe flatulence and regurgitation with any bending job. Occasionally there were bouts of vomiting. Radiographs in 1954 confirmed the presence of a hiatal hernia, which was at first treated medically. In 1957, however, because the symptoms persisted, he was referred for surgical treatment. His past history was non-contributory.

Physical examination showed a well-built man of 14 st. (88.9 kg.). His blood-pressure was 130/90 mm. Hg, and no physical abnormalities were detectable. As there was clear *x*-ray evidence of hiatal hernia (Fig. 1), oesophagoscopy on this occasion was not performed.

Operation

On May 29 the left chest was opened through the left eighth-rib bed. After division of the inferior pulmonary ligament the oesophagus was isolated. This proved unexpectedly difficult because of a large unsuspected tumour which lay within the oesophageal wall, just beyond the upper limit of his large hiatal hernia. After the oesophagus was dissected from the posterior mediastinum, closer inspection showed that the tumour was lobulated, was almost the size of a cricket ball, almost completely encircled the oesophageal lumen without greatly narrowing it, and extended at least 9 cm. up the wall of the lower oesophagus. A small radial incision was made in the diaphragm, and inspection showed no enlargement of the regional lymph nodes along the course of the left gastric artery. Because the growth lay strictly within the oesophageal wall and was in no way attached to any adjoining structure, the most likely diagnosis was thought to be a leiomyoma of the oesophagus.

FIG. 1.—Barium swallow, showing hiatal hernia without oesophageal obstruction.

Excision of Tumour.—A vertical incision was made through the oesophageal muscle layer and the tumour found to lie in the submucosa. With care it was gradually enucleated. There were several ramifications which extended upwards and downwards from the main tumour mass, without invading the mucous membrane. The tumour was ultimately dissected free and several small vertical mucosal splits were closed with fine silk sutures on atraumatic needles. The overlying thickened muscle wall of the oesophagus was finally approximated with interrupted No. 0 chromic catgut sutures placed in two layers.

Repair of Hiatal Hernia.—The hiatal hernia was next reduced by passing the catheter sling around the oesophagus down through the hiatal opening and out again through the radial incision in the diaphragm. The dissected crural fibres of the diaphragm were then approximated behind the oesophagus with four double No. 4 silk sutures. The oesophagus was also sewn to the diaphragm in the hiatal region with a series of interrupted No. 2 silk sutures. The small exploratory incision in the diaphragm was closed with two layers of double No. 2 silk sutures, and the chest wall was closed over water-seal drainage.

Progress

The patient was kept on intravenous fluids for two days, after which he took increasing amounts of fluid by mouth, and solid food after 10 days. He was discharged fit 12 days after operation.

FIG. 2.—Leiomyoma discovered in lower third of oesophagus when repairing the hiatal hernia.

Pathological Report.—The specimen consisted of a lobulated tumour, 9 by 5 by 2 cm., which had been excised from the submucous layer of the lower oesophagus. Histologically it was composed of interlacing bundles of smooth-muscle fibres which showed no evidence of malignancy (Fig. 2). This was a leiomyoma of the oesophagus.

Follow-up.—When seen two years later he was well. A check oesophagoscopy on June 4, 1959, showed satisfactory function of the cardia, and no evidence from the mucosal surface to suggest any recurrence. Check barium swallow also showed no evidence of tumour recurrence.

Case 2

A labourer aged 59 was admitted to hospital on November 21, 1957, for surgical treatment of a hiatal hernia. He first consulted his private practitioner on July 20,

1957, complaining of severe substernal pain and sweating. For 20 years he had noticed retrosternal "heartburn," generally initiated by leaning forward or lying down. Over the past six months it had become more frequent, occurring as often as two or three times a day. It was relieved by taking sodium bicarbonate or the proprietary preparation "rennies." He had severe flatulence. At no time did he complain of dysphagia. There was no history of melaena, haematemesis, or any other complaint referable to the alimentary system.

In addition to his heartburn, he complained of palpitations while working, together with a crushing precordial pain suggestive of angina of effort which doubled him up and at times radiated down his left arm. His past history and family history were non-contributory.

On physical examination he was a somewhat obese man weighing 13 st. 2 lb. (83.5 cm.). His alimentary, cardiovascular, respiratory, genito-urinary, and central nervous systems were all normal. His blood-pressure was 170/100 mm. Hg, his electrocardiogram was normal, and an oesophagogram showed reflux from the stomach into the lower oesophagus with a hiatal hernia.

Oesophagoscopy on November 22 revealed a lax cardia with no normal sphincteric control. There was free regurgitation of gastric juice into the lower oesophagus without any severe ulceration of the mucous membrane. The oesophagoscope passed easily through into the stomach.

A provisional diagnosis of reflux oesophagitis and possible coronary insufficiency was made, and repair of the hiatal hernia advised to relieve symptoms.

Operation

On November 27 the left pleural cavity was opened through the left eighth intercostal space. Pleural adhesions over the left lower lobe were divided. After division of the inferior pulmonary ligament the oesophagus was isolated in the posterior mediastinum and raised with a catheter sling. Examination at this stage showed not only a hiatal hernia that admitted all the fingers of one hand but also a large lobulated tumour growing within the wall of the lower third of the oesophagus. The tumour arose from the left side of the oesophagus; it penetrated through the musculature and grew in a lobulated fashion throughout the peri-oesophageal tissue of the posterior mediastinum. In its fresh state it measured 7 by 3 by 1.5 cm. It was not firmly adherent to any structure, nor was there any lymph-node enlargement. It had all the pathological characteristics of an extramucous, extramural leiomyoma.

A small radial incision was made in the diaphragm; the hernial sac was opened and the crura of the diaphragm defined. At this stage, after a vertical incision in the oesophageal wall, the tumour was further dissected and was found to extend down to, but not through, the mucous layer of the oesophagus. It was carefully excised without injuring the mucous membrane, and the oesophageal muscular layers were then approximated with interrupted No. 2 silk sutures, placed at 1-cm. intervals. Thereafter the hiatal hernia was repaired by a technique similar to that in Case 1.

Progress

Convalescence was complicated by urinary retention, secondary to minimal lateral-lobe prostatic hypertrophy. At first this was treated by an indwelling Foley catheter. Ankle oedema was detected on December 7, and a further E.C.G. showed a left bundle-branch block.

Some 19 days after this thoracic operation the patient was transferred to the urological department, where a transurethral resection of a median-bar prostatic obstruction was performed. Four days later, while shaving in the bathroom, he dropped dead. Necropsy revealed signs of heart failure secondary to a recently healed intraventricular myocardial infarct, with pulmonary oedema, small bilateral hydrothoraces, and two small pulmonary artery thromboses in the right lower lobe. In addition the myocardium was hypertrophied, there was severe atherosclerosis of the right and left coronary arteries, and there were two infarcts of the right kidney.

The specimen consisted of a lobulated tumour measuring 6 by 2.5 by 2 cm. The cut surface had a whorled, homogeneous appearance, with occasional flecks of calcium. Histological section showed that the tumour comprised smooth muscle together with a large amount of collagen. This was a leiomyoma of the oesophagus.

Discussion

The occurrence of unsuspected tumours in the oesophagus may be considered rare when viewed in the light of Moersch and Harrington's (1944) findings of 44 cases in 7,459 routine necropsies, yet Meissner's (1944) finding of 46 leiomyomas in 50 random careful necropsy examinations of the stomach suggests far greater frequency

Malignant tumours in association with hiatal hernias are regularly reported. Carcinomas are the commonest. The relevant literature was cited by Pack *et al.* (1952) when describing two further cases. Robb (1954), in reviewing 138 hiatal hernias, found two cases with an associated carcinoma of the oesophagus, as well as four others with carcinoma of the stomach and one from the sigmoid colon. Adler and Rodriguez (1959) found that 21 (2.5%) out of 814 hiatal hernias had an associated malignancy. Nine were oesophageal, of which two were in the upper third of the oesophagus, one in the middle, and six in the lower third. Twelve were gastric, eight being at the cardia and four spread more distally.

I have encountered five tumours—two carcinomas of the oesophagus, a lipoma, and these two leiomyomas—in a series of 75 hiatal hernias treated surgically. In addition, a fibrosarcoma has been described elsewhere—detected one year after repair of a hiatal hernia (Borrie, 1959).

Benign tumours of the oesophagus fall into two pathological and clinical groups—namely, those arising from the mucosa, "intraluminal tumours," and those arising from extramucosal tissue, "intramural tumours." These latter may remain sessile and entirely intramural, or they may extend extramurally. The mucosal or intraluminal benign tumours may be lipomas, polyps, adenomas, haemangiomas, myofibromas, and fibrolipomas as reported by Moersch and Harrington. Their intramural tumours included leiomyomas, myomas, and cysts. Other tumours reported include neurofibromas and osteochondromas.

The commonest benign oesophageal tumours are leiomyomas. Their association with hiatal hernias has rarely been recorded in the past. Schafer and Kittle (1947) reported one that gripped the entire lower oesophagus like a fist; there was an associated gastro-hiatal hernia, and it required a partial oesophago-gastrectomy. Goldman and Masters (1950) described a similar case.

The age incidence of leiomyomas corresponds to the maximum age incidence of hiatal hernias. Though Rose (1936) in reviewing 49 cases, found the 60–70 age-group most affected, in Myers and Bradshaw's (1951) series of 42 cases the ages ranged from 1½ to 66 years. Sweet *et al.* (1954) recorded a range from 19 to 67 years in patients treated surgically, with an average of 41.2 years. Further, they reported 25 cases in men and 22 in women, indicating that the sex incidence was almost equal.

The commonest site for leiomyomas is the lower oesophagus, so that again they can be expected to occur from time to time in association with the commonest lower oesophageal lesion—namely, a hiatal hernia.

These tumours vary in size from a match-head to one weighing 1,420 g. as reported by Kenney (1953). They are firm and may be round, nodular, or lobulated. Though they can be localized, they tend to encircle the oesophagus and spread upwards in the submucosal plane. Only if there is actual narrowing of the oesophageal lumen will dysphagia occur. Because the oesophageal lumen was not grossly occluded, the two patients in this report had symptoms referable only to their hiatal hernias. Neither barium studies nor oesophagoscopy suggested the presence of an intramural tumour.

The Approach to Hiatal Herniorrhaphy

Several surgical approaches to hiatal herniorrhaphy have been devised. Harrington (1955) has favoured the abdominal approach, Allison (1951) the left thoracic approach, while Collis *et al.* (1954) have advocated an abdomino-thoracic approach. I have on one occasion successfully repaired such a lesion through the right pleural cavity (Borrie, 1958).

Suffice it to say that as a guiding principle the route chosen for this operation should be the one which allows of greatest flexibility—and especially when unsuspected tumours can be discovered by chance in the lower third of the oesophagus or upper third of the stomach. This pathological fact strongly supports the view that the route that will allow inspection of both the lower oesophagus and the upper stomach should be used wherever possible, and that opportunity be taken to inspect the foregut on both sides of the diaphragm. This ideal is possible only via a left transthoracic approach with division of the diaphragm. Had these two patients been treated by the abdominal route, these tumours could not have been detected during the standard transabdominal repair and therefore would have been left to grow until the inevitable onset of dysphagia.

At operation the lobulated appearance of the lesion confined to the oesophagus with no extension into surrounding structures and no lymph-node invasion made the diagnosis of an intramural leiomyoma tolerably certain. Conservative removal was therefore chosen, and a vertical incision through the outer muscle layers gave easy access to the loose submucosal plane in which it lay. Careful dissection was required to avoid injury to the mucous layer. Thereafter the hiatal hernia was reduced and repaired by standard techniques.

Summary

The chance finding within a seven-months period of two leiomyomas of the lower third of the oesophagus during transthoracic repair of two apparently simple sliding hiatal hernias emphasizes again that hiatal hernias do sometimes occur in association with lower oesophageal tumours—benign as well as malignant—that some of these tumours may be undetectable despite barium studies and oesophagoscopy until operation, and that only by the left transthoracic route can they readily be detected and treated.

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EFFECT OF PREDNISOLONE IN BANCROFTIAN ELEPHANTIASIS

BY

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Conflicting reports on the place of steroids in the treatment of Bancroftian elephantiasis have suggested that further trials were necessary before their efficacy in the treatment of this condition could be ascertained. Using corticotrophin, McFadzean (1953) was unable to detect any improvement in his cases in West Africa, and Subramaniam and Mohammed (1957), in India, reported only temporary improvement with cortisone. Markell and Kerrest (1955), in Tahiti, reported considerable improvement with cortisone, and Laigret, March, and Kessel (1957) obtained good results when cortisone or prednisone was combined with bandaging and Unna's paste.

The present communication is a report of a trial in which prednisolone was given to seven persons with Bancroftian elephantiasis due to periodic *Wuchereria bancrofti*.

Material and Methods

The diagnosis of Bancroftian elephantiasis is sometimes difficult, as laboratory tests are rarely of help and clinically the condition is often indistinguishable from other causes of tropical elephantiasis (Jordan, Trant, and Laurie, 1956). Patients were selected for the present series if they came from areas of Tanganyika where Bancroftian infection was known to be common. The condition had been present for periods ranging from one to eight years, and the severity of the disease varied from slight to severe. In some advanced cases the skin was verrucose, and in every case was thicker than normal. In three patients the disease was bilateral.

All patients were examined and questioned with regard to possible peptic ulceration and chest disease. Where necessary an *x*-ray examination was made. The fluid intake and urinary output were measured for a few days before treatment in order that any diuresis that might occur during treatment could be more accurately assessed.

The legs of all patients were measured at four levels —mid-thigh, mid-calf, at the ankle, and round the foot— before and after treatment. Measurements were made at preselected points at fixed distances from the anterior superior iliac spine. Accuracy in measuring the circum-

ference of limbs on a number of occasions, even at selected points, leaves much to be desired. In some cases an apparent reduction in the size of the limb was noted at one level, while no reduction, or even an increase, was noted at another site. In order to obtain an overall picture the four measurements were added. This single figure was then compared with subsequent measurements.

Treatment

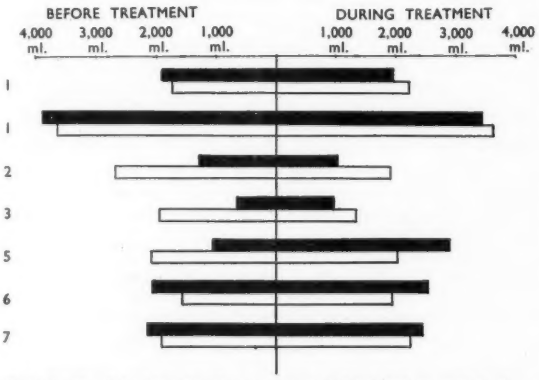
The first three patients were confined to bed during treatment, but the fourth, an African medical student, was treated as an out-patient, and his early elephantiasis improved considerably. In view of this success, and the fact that the cases in the successful series had all been out-patients, subsequent patients were encouraged to walk about during treatment.

Treatment was started with twice-daily injections of 1 ml. (25 mg.) of prednisolone, followed by 1 ml. a day in two doses for 25 days. The drug was then slowly withdrawn.

Side-effects were noted on two occasions. Patient 1 (who was confined to bed) developed palpitations and pain in his chest. A pericardial rub developed, but this cleared in a few days without the drug being discontinued. A second course of treatment with the patient ambulant was completed uneventfully. Patient 6 complained of palpitations, but no physical signs developed. The drug was continued, and the patient, who had been ambulant, was made to rest more. The condition cleared before the end of treatment.

Results

In only one patient (Case 1) was a slight diuresis noted, and it is interesting that this also occurred during a second course of treatment (see Chart). The result



Fluid intake (black) and urinary output (white) before and during treatment. (Patient No. 4 was treated as an out-patient and no figures are available.)

of limb measurements, before and after treatment and at follow-up, are shown in Table I. Though there was a slight improvement in limb measurements in most patients at the end of treatment, the medical student referred to above was the only one in whom a lasting reduction in the size of limb was obtained—the measurements of the two limbs being almost identical at the end of treatment, and the thickened skin was normal. Eight months after treatment the condition had not deteriorated.

TABLE I.—*Results of Treating Elephantiasis with Prednisolone (Measurements in Inches)*

Case No.	Leg	Sum of Measurements from 4 Levels			Time of Follow-up	Comment
		Pre-treatment	End of Treatment	Follow-up		
1	L.	64·6	60·5	66·1	6 months	Bilateral disease. 1st course. Treated in bed
1st course	R.	65·1	62·3	68·2		
2nd course	L.	66·1	64·7	67·5	2 ,,	Ambulant
	R.	68·2	67·5	70·5		
2	L.	54·4	54·5	53·4	3 ,,	Rt. leg diseased. Treated in bed
	R.	65·6	61·1	67·2		
3	L.	62·8	61·7	62·7	12 ,,	Lt. leg diseased. Treated in bed
	R.	60·8	61·4	61·2		
4	L.	57·3	54·3	53·5	8 ,,	Lt. leg diseased. Ambulant during treatment
	R.	55·8	54·3	55·5		
5	L.	60·9	61·0	62·0	4 ,,	Bilateral disease. Ambulant
	R.	56·6	56·9	56·8		
6	L.	52·7	50·0	52·3	6 ,,	Bilateral disease. Ambulant
	R.	52·2	51·5	51·9		
7	L.	50·5	49·3	No follow-up		Rt. leg diseased. Treated in bed
	R.	55·2	53·7			

At the end of treatment a slight reduction in the size of the limbs—elephantoid and normal—was noted in all but one of the other patients. The reduction was greatest in those who were confined to bed during treatment. The prednisolone cannot be claimed to have caused this reduction, as a reduction invariably occurs if a patient with elephantiasis is confined to bed, whether or not treatment is given. On becoming ambulant, however, the limbs returned to their previous state, and at follow-up examinations, 2 to 12 months later, limb measurements were no less than before treatment.

Effect of Prednisolone on Clinical Condition

Markell and Kerrest (1955) suggest that the total of 540 mg. of corticotrophin given over a period of eight days by McFadzean was insufficient to bring about a reduction in the size of the elephantoid leg. They gave 100 mg. of cortisone daily for 30 days, and measurements of the limbs showed that five out of seven cases continued to improve for eight months, and only one case failed to respond to treatment. In addition to the circumference of the leg being reduced, the limb was softened and the patients—treated as out-patients—reported diuresis occurring with treatment.

The results of Laigret *et al.* (1957) are difficult to evaluate, as drug therapy was combined with Unna's paste bandages and no comparable series showing the effect of these methods alone is given. Thooris (1953), however, reported good results with Unna's paste bandages.

Sumbramaniam and Mohammed (1957) reported a temporary improvement in two out of nine cases treated with 60 mg. of cortisone a day for seven days, followed by a reduced dose of 30 mg. a day for 15 days, then 15 mg. daily for a further 10 days.

If Markell and Kerrest are correct in their claim that the dose must be high, it is difficult to see why the prednisolone given in the present series failed to produce improvement, as the dose given was equivalent to the dose of cortisone used by them. Since the cases in their series were treated as out-patients, and the one successful case in the present series was ambulant during treatment, it is possible that the drug acts better under these conditions. One might postulate that muscular contractions facilitate flow in the lymphatic vessels, and that if a block exists in the gland or vessel, and is removed either partially or completely by the drug,

the fluid accumulated in the limb would pass into the circulation and eventually be excreted, leading to a diuresis.

It is interesting to note that the series in which these drugs failed to alleviate the swelling of elephantiasis were from areas in which the microfilariae show periodicity—East and West Africa and India. The successful results are from an area where the microfilariae show no periodicity—Tahiti.

Effect of Prednisolone on Microfilaraemia

It might be argued that in elephantiasis the action of prednisolone is not the same as that of cortisone. One patient in the present series, however, had a low-density microfilaraemia, and during the third week of treatment the number of microfilariae increased (Table II) as they did at the same time in one of Markell's cases.

TABLE II.—*Increase in Microfilarial Density During Prednisolone Therapy*

Date	Comment	Quantity of Blood	No. of Slides Positive	Total Microfilariae
1/12/57	Before treatment	2 thick unmeasured smears	1	1
9/12/57	,, ,,	6 × 20 c.mm.	0	0
16/12/57	Prednisolone started	5 × 20 c.mm.	0	0
8/1/58		4 × 20 c.mm.	3	3
14/1/58	,, finished	6 × 20 c.mm.	5	10
21/1/58		6 × 20 c.mm.	5	7
24/1/58		6 × 20 c.mm.	3	3
18/3/58		5 × 20 c.mm.	0	0

Markell and Kerrest (1955) claimed that this was due to the release of microfilariae from blocked lymphatics. If this is a true explanation of the increased microfilarial density, the fact that it occurred with prednisolone suggests that this drug should lead also to the passage of fluid through previously blocked or partially blocked lymphatics, with a reduction in size of the limb. A slight temporary reduction did occur during treatment, as in most of the other cases, but the swelling recurred as soon as the treatment stopped and the patient was fully mobile.

It has been suggested that the absence of microfilaraemia in most cases of elephantiasis is due to the embryos being unable to pass the fibrosed lymph nodes (Acton and Rao, 1933 ; Napier, 1944). This implies that live adult filarial worms in elephantiasis are confined to the diseased limb. Bahr (1912) and O'Connor and Hulse (1935), however, found that in infected persons at post-mortem examination many of the lymph nodes in the body may be invaded.

If, in spite of this, the above is a correct explanation of the absence of microfilaraemia in cases of elephantiasis, continuous reinfection of the individual in endemic areas might be expected with the later development of microfilaraemia. In a series of elephantiasis cases reported by Galliard, Mille, and Robinson (1949) there was, however, no increase in the microfilaraemia rate in the higher age-groups of a series of elephantoid patients. Unpublished work in Tanganyika confirms this, and it suggests that reinfection does not take place. This may indicate that immune processes, which may be the cause of, or be caused by, the elephantiasis, are operative, and may be responsible for the very low incidence of microfilaraemia in these cases.

It is suggested that, in elephantiasis, steroids may alter the immune reactions and prevent the destruction of microfilariae during treatment, but that, when treatment ceases, normal immune processes become manifest and the numbers of microfilariae are reduced again. Support for this hypothesis is provided by the work of Markell and Lewis (1957), who showed in rats that cortisone reduced the immunity to subsequent reinfection with trichinellae.

Among hospital in-patients, aborting females and persons with trauma were found to have a higher incidence of microfilaraemia than patients with other complaints. It was suggested that this might be due to products from damaged tissues (Jordan, 1954). In view, however, of the effect of steroids on microfilaraemia (at least in the case of elephantiasis) it seems more likely that it is due to hydrocortisone, the production of which is increased after trauma and doubled during pregnancy (Cope, 1959).

Summary

Prednisolone was given to seven persons with elephantiasis. In one early case the swelling of the limb and the condition of the skin improved with treatment.

Microfilariae in one patient increased in numbers during treatment but became fewer after treatment. The cause of this is discussed.

Acknowledgments are made to the Administrator, East Africa High Commission, for permission to publish this paper ; to Mrs. M. Pedley, nursing sister, for her co-operation ; and to Scherag (Pty.) Ltd. for the supply of " meticortelone " (prednisolone) used in this work. (The substance of this paper formed part of a thesis accepted for the degree of Doctor of Medicine by London University.)

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" Science is inevitable, not only because its methods are the only proved methods for increasing the understanding of the world in which we have our being, but also because even those who are not concerned with this understanding make it inevitable through their demands for the physical fruits of science. So it is that, while the scientific method may, at times, have had to be defended, science as such has never had to sell itself—for the good reason that it enjoys an infinite 'sellers' market.' Science, we can say, is inevitable, even though the social consequences of its advances and of the application of these advances have to be entrusted to the future, an enlightened and impartial judge, as de Tocqueville wrote, but one who sits, alas, always too late." (Professor Sir Solly Zuckerman, F.R.S.: Stephen Paget Memorial Lecture. *Conquest. The Journal of the Research Defence Society*, January, 1960.)

MONTHLY RHYTHM OF LIBIDO IN MARRIED WOMEN

BY

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Since classical times there has been discussion on the existence or non-existence of variations in libido in women during the menstrual cycle.* This discussion reached its peak in the nineteenth and early part of the present century. The main difference of opinion lay between those who believed that there was increased libido in association with menstruation itself—that is, just before, just after, or during, or various combinations thereof (for example, Campbell, 1891; Kossmann, 1903; Havelock Ellis, 1910)—and those who denied the existence of any monthly enhancement of sexual desire in women (for example, Fürbringer, 1918).

The more recent literature continues to show marked differences of opinion. Thus Corner (1952) maintained that libido is maximal just before or just after menstruation, whereas Stopes (1937) considered the monthly rhythm to have two peaks, one just before menstruation and the other at mid-cycle. On the other hand, Eckstein and Zuckerman (1956) stated that "sexual behaviour in women very rarely manifests any rhythmic pattern." However, according to Swyer (1954), "Psychic changes occur throughout the menstrual cycle. So great are the variations in different individuals that generalizations are difficult to draw. Thus, whereas some women lose all or most of their libido during the menstrual period, others may feel more highly sexually excitable at this than at any other time. Some women experience their highest libido at about mid-cycle—that is, near the time of ovulation, but, though this would be expected on biological grounds, it is far from universal."

The wide differences in viewpoint found in the literature can be attributed to a number of causes: (1) the masking of rhythmic variations in sexual feeling by an overlay of various social and psychological factors, such as the demands of a young family, fatigue, etc. (Ellis, 1910); (2) differences between maximum and minimum libido being much less marked during the monthly cycle in humans than in other primates (Corner, 1952); (3) the reluctance (until recently) to question women directly on this subject (Fürbringer, 1918); (4) individual variability (Swyer, 1954); and (5) the frequent lack of a statistical approach.

Present Investigation

While engaged in marital and sex problem work, I noted a certain pattern in the answers given to occasional questions concerning monthly variations in libido. This stimulated a more organized inquiry among women attending either the contraceptive clinic at University College Hospital or the Caversham Group General Practice. The inquiry covered successive patients who came for contraceptive advice only and who had been married for at least one year. The only deliberate exclusions were obvious marital and sex problem cases. At the same time as the questions were asked concerning libido, the opportunity was taken to discover the extent of knowledge of the "safe period" (Ogino, 1934; Knaus, 1934)—that is, the time during the menstrual cycle when coitus is believed to be unlikely to lead to conception. It was thought possible that such knowledge on the part of the patient might be associated with variations in libido.

After ascertaining the patient's willingness to co-operate, I asked her to tell me her name, age, years married, parity, frequency of sexual intercourse, frequency of orgasm; then two sets of questions were asked: (1) "Do you notice if you feel more like having intercourse at certain times during the month (menstrual cycle)? Is the time related to your period (menstruation)?"; and (2) "Do you know what the 'safe period' is? When do you believe it to be?"

There were 123 patients in the study. They were aged from 19 to 49 years, and had been married from 1 to 22 years.

Results

Table I shows that in 59% of the patients the time of maximum libido was closely associated with that of menstruation. Only 6% reported this maximum to be in the middle of the cycle, and so at about the time of ovulation, when fertility would be expected to be maximal. In 34% libido was not reported to be greater at any particular time of the menstrual cycle.

TABLE I.—*Part of Menstrual Cycle in Which Maximum Libido was Experienced*

Time of Maximum Libido	No.	Percentage
Associated with menstruation	70	59
Just before	26	22
,, after	26	22
,, before and just after	9	8
During	4	3
Miscellaneous	5*	4
Middle of cycle	7	6
No particular time	40	34
Total	117†	99

* One before and during menstruation; two at the start; one just before, during, and just after menstruation; and one just before menstruation and at mid-cycle.

† The 123 study patients less 6 who did not answer the questions.

In the 59% of patients who associated their maximum libido with menstruation, 22% experienced it just before, 22% just after, 8% just before and just after, and 3% during, menstruation.

The patients (excluding 2 who answered incompletely) were then subdivided into those married from one to five years and those married for more than five years: 57% of the 60 recently married women and 64% of the 55 who had been married longer reported their maximum libido to be associated with menstruation, while 38% and 29%, respectively, reported this to be at no particular time (for the remaining 5% and

TABLE II.—*Knowledge of the "Safe Period" Claimed by the Patients*

Total who Replied	Knowledge of "Safe Period"		
	"No"	"Yes"	
		Believed it to be at Mid-cycle	Believed it to be Around Menstruation
115* (100%)	50 (43%)	11 (10%)	54 (47%)

* The 123 study patients less 8 who did not answer the questions.

*The menstrual cycle is measured from the first day of one menstruation to the first day of the next.

7%, respectively, it was at mid-cycle). The differences between the figures for the recently and the longer-married groups are not statistically significant.

Table II shows that 43% were ignorant of the "safe period," and that of those who knew of it, one-sixth, or 10% of the total, placed it at mid-cycle—which is generally believed to be the most fertile period. On the other hand, 47% of the total placed the "safe period" in association with menstruation (mainly shortly before and/or just after), which is, on the whole, accepted as a relatively safe time.

Table III links the answers to the two sets of questions. It shows that the proportion of the women who experienced maximum libido in association with menstruation was similar whether they believed this to be a safe time or not.

TABLE III.—*Timing of Maximum Libido According to Patient's Knowledge of the "Safe Period"*

Time of Maximum Libido	Placing of "Safe Period" by Patient							
	Associated with Menstruation		At Mid-cycle		No knowledge		Total	
	No.	%	No.	%	No.	%	No.	%
Associated with menstruation	30	*60*	4	*44*	31	*62*	65	*60*
Middle of cycle	4	*8*	0	*0*	2	*4*	6	*6*
No particular time	16	*32*	5	*55*	17	*34*	38	*35*
Total ..	50	*100*	9	*99*	50	*100*	109*	*101*

* The 123 study patients less 14 who did not answer one or other set of questions.

Discussion

The present comparatively small series of healthy married working- and middle-class women in London has exemplified all the varieties of monthly enhancement of sexual desire previously described. Their relative prevalence is, however, of much interest. Most of the women experienced a distinct monthly rhythm, but a substantial minority did not. Nearly all the former described the increased libido to be around the time of menstruation; only a very small proportion felt maximum desire at the time when they were most likely to conceive—namely, at mid-cycle. This contradiction between time of maximum desire and likelihood of conception is a most striking finding. It is interesting to reflect that in the past such a contradiction did not necessarily appear to exist, since the estimated time of ovulation has undergone many changes—some authors believed it to be just after menstruation, thus often coinciding with maximum libido.

Various authors (Fürbringer, 1918; Van de Velde, 1947; and others) have considered that increased sexual desire just after menstruation was due to temporary abstinence during the menses. Doubt is cast on this explanation by the frequency with which this increase occurred in the present series just before menstruation.

The present results are broadly in agreement with those obtained by Davis (1929), by the postal-questionary method, on sexual desire in American women. Her data, however, were concerned only with the time up to marriage.

Knowledge of the so-called safe period was claimed by only half the group. This may reflect the ready availability in this country of other (and more reliable) contraceptive methods. Of those who claimed this knowledge, most placed the safe period at a time when conception is generally believed to be least likely, though a minority placed it around the time of ovulation. Moreover, knowledge of the safe period does not appear to have been a factor in the occurrence of increased libido around the time of menstruation.

Summary

123 healthy married women seeking contraceptive advice were asked whether they had noticed any increase in sexual desire during their menstrual cycle. 59% answered that enhancement occurred around the time of menstruation, when fertility would be expected to be minimal; only 6% reported increased libido around mid-cycle (ovulation time), when fertility is highest; and 34% reported no rhythmically occurring increase of sexual desire. The contradiction between the time of maximum desire and the likelihood of conception was a most striking finding.

The women were also questioned about knowledge of the "safe period." 43% were ignorant of this; 47% placed it around menstruation, which is generally accepted as the least fertile time; and 10% said that it was at mid-cycle, when conception is most likely.

Knowledge of the safe period does not appear to have had any influence on enhancement of sexual desire during the monthly cycle.

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"The prime function of language is to communicate thought or feeling intelligibly, and for most of our needs simple, concise, lucid, logical expression is enough. But go to the meeting of a committee and what do you hear? Often raw slices of maundering, repetitive, ungrammatical, formless jargon. Look at the agenda of many academic committees, at the letters and documents which pour in upon one from departments of government, from advertisers, from candidates. Diffuse, tedious and turgid. Why are they not easy and free and straightforward? Too many people will not take the trouble to keep to a brief, terse, controlled style and to cut out the unnecessary and falsely impressive. With Hazlitt I declare that 'I hate anything that occupies more space than it is worth . . . and I hate to see a parcel of big words without anything in them.'" (*Royal Free Hospital Journal*, January, 1960. Inaugural Address: "The English Language," by Dr. John Lockwood, Master of Birkbeck College.)

THYROTOXICOSIS AND ADDISON'S DISEASE IN SAME PATIENT

BY

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The association of Addison's disease and thyrotoxicosis in the same patient is uncommon. A case was described by Rupp and Paschkis (1957), but they could find only eight previously reported cases in which such a double diagnosis appeared to be acceptable. A case showing this combination of diseases is described below and illustrates the influence of the thyroid gland on adrenal cortical function.

Case Report

A married woman aged 53 was involved in a motor-car accident in February, 1957, sustaining no injury. In August of that year she began to "shake like a dancing doll," so that at times she was unable to dress herself and became very irritable. Six months later her eyes became prominent and she noticed a swelling in her neck. During the year before admission she noted increasing pigmentation of the skin, loss of appetite, and severe nausea; and over the last four months she lost 2 st. (12.7 kg.) in weight.

On admission to hospital in January, 1959, she was agitated; blood-pressure 130/60; weight 7st. 6 lb. (47.2 kg.); temperature 100.8° F. (38.2° C.); pulse 140. Increased pigmentation was present, especially over the face, chest, and axillary folds, and patches were visible on the buccal surface of the cheek and soft palate. A diffuse smooth enlargement of the thyroid gland, a well-marked exophthalmos, and a fine tremor of the hands were present.

Investigations.—Haemoglobin, 10.8 g./100 ml.; white blood count, 11,500/c.mm. (neutrophils 42%, lymphocytes 48%, monocytes 5%, eosinophils 5%); E.S.R., 25 mm. in one hour (Wintrobe). An electrocardiogram showed sinus tachycardia with ST depression in leads II, III, aVF, V5-7. Radiological examination of the lungs revealed a calcified primary complex but no other evidence of tuberculosis, and examination of the abdomen showed no evidence of calcification in the adrenal area.

The patient remained febrile, and two days after admission she was moved into a single room, but complained that she could not sleep owing to a noisy heating installation. She became progressively more restless and agitated, mentally coufused, and resentful of any interference, and threatened to take her own discharge from the hospital. She then began to vomit small quantities of bile-stained material, the pulse became very weak, and the systolic blood-pressure suddenly fell to 70 mm., the diastolic pressure being unobtainable. At this time the serum sodium was 132 mEq; potassium 6.0 mEq; bicarbonate 25 mEq; serum cholesterol 163 mg./100 ml.; and blood-sugar 98 mg./100 ml. A diagnosis of Addisonian crisis precipitated by severe thyrotoxicosis was made, and she was treated with intravenous dextrose-saline, hydrocortisone hemisuccinate intravenously to a total of 400 mg. in 12 hours, and 5 mg. of deoxycortone intramuscularly. Within a few hours of starting treatment she was much improved, was again rational though still restless, and the blood-pressure had risen to 140/60. Intravenous therapy was subsequently replaced by oral cortisone, 25 mg. b.d., fludrocortisone, 0.25 mg. daily, and propylthiouracil, 200 mg. t.d.s., for the next two weeks, during which she continued to improve though remaining febrile. In order to continue investigations of thyroid and adrenal function all treatment was then discontinued apart from fludrocortisone, 0.25 mg. b.d.

Ten days later the following tests were performed. *Thyroid function*:—B.M.R. +38%; plasma protein-bound radioactive iodine, 1.4% of administered dose per litre at 48 hours (normal <0.4%). *Adrenal function*:—*Before corticotrophin*: urinary 17-ketosteroids, 0 (normal 5–15 mg./24 hours); urinary 17-ketogenic steroids, 4 mg./24 hours (normal 8–18 mg./24 hours); plasma free 17-hydroxycorticoids, 3 μg./100 ml. (normal 6–20 μg.). *After corticotrophin* (corticotrophin-zinc 40 units intramuscularly b.d. for two days): urinary 17-ketosteroids, 0 each day; urinary 17-ketogenic steroids, 4 mg. and 1 mg./24 hours; plasma free 17-hydroxycorticoids, 0 (on two successive days four hours after corticotrophin).

Treatment was resumed with cortisone acetate, 37.5 mg. daily, and fludrocortisone, 0.1 mg. daily. Carbimazole, 10 mg. t.d.s., was substituted for propylthiouracil; there was no recurrence of the pyrexia. One month after discharge from hospital she was very well, having gained 14 lb. (6.4 kg.) in weight. The pulse rate was 80 and the blood-pressure 170/90.

Discussion

The diagnosis of hyperthyroidism in this patient was made clinically and was confirmed by a raised basal metabolic rate and increased protein-bound radioactive iodine. The diagnosis of Addison's disease was suggested by the presence of increased pigmentation and anorexia, and confirmed by the low steroid levels in plasma and urine.

In uncomplicated hyperthyroidism urinary 17-hydroxycorticoids are either normal or slightly raised (Levin and Daughaday, 1955), and plasma 17-hydroxycorticoids are normal (Levin and Daughaday, 1955; Wallace *et al.*, 1955). In this patient the low or absent 17-hydroxycorticoids and 17-ketosteroids in urine and plasma, together with a failure of the steroid levels to rise after the administration of corticotrophin, indicated primary adrenal insufficiency.

It has long been known that the administration of thyroxine to patients with Addison's disease may precipitate adrenal crisis (Lerman and Stebbins, 1942), and recent investigations into the influence of the thyroid on adrenal cortical function have thrown further light on these clinical observations. Levin and Daughaday, (1955) and Peterson (1958) have shown that in cases of hyperthyroidism there is a greatly increased metabolism of hydrocortisone, and this is normally accompanied by an increased production by the adrenal cortex, since plasma levels of hydrocortisone remain within the normal range.

This relationship, however, may be disturbed either in the event of the metabolism of hydrocortisone being so great as to overwhelm the productive capacity of a normal adrenal, such as may be postulated to occur in a thyroid crisis, or, more certainly, when coexistent disease of the adrenal cortex is present.

In the above case signs of Addison's disease appeared to develop after the onset of thyrotoxicosis. During an exacerbation of the hyperthyroidism the adrenal cortex was presumably unable to meet the demand for an increased output of hydrocortisone, and an adrenal crisis occurred which responded rapidly to the intravenous administration of hydrocortisone. Since the hyperthyroidism has been treated by antithyroid drugs the adrenal insufficiency has been controlled by steroid therapy in conventional dosage without difficulty.

Summary

A case is described in which both hyperthyroidism and Addison's disease were present. Exacerbation of hyperthyroidism resulted in an adrenal crisis.

The relationship between thyroid and adrenal cortical function is discussed.

We thank Dr. J. R. Nassim for permission to publish details of this case, admitted under his care.

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Medical Memoranda

Response of Favus to Griseofulvin

Favus of the scalp is an intractable disease due predominantly to *Tricophyton schoenleini*, though *T. quinckeanum* may also be responsible for the infection. In the past the choice in therapy has been *x*-ray epilation and vigorously applied local medicaments, but the advent of griseofulvin and its success in the management of other fungous infections of skin, hair, and nails has caused speculation about whether favus, too, will respond. Sulzberger and Baer (1959) refer to this gap in our knowledge, and Pardo-Castello *et al.* (1959), while hailing the drug as the treatment of choice in all superficial mycoses, omit all mention of favus. It seemed to us that an account of the progress we have observed in two cases of favus under treatment with griseofulvin might be of interest.

CASE 1

A married woman aged 38 attended as an out-patient with a view to obtaining a wig. She complained of having had baldness for 36 years. This was diffuse, with crusting and scarring mainly round the sides of the scalp and on the occipital region, where typical yellowish scutula were also present (Fig. 1). Bright-green fluorescence was noted under Wood's light, most vivid on the occiput. Direct microscopy revealed the presence of fungus in hairs, and *T. schoenleini* was grown on culture.

Blood counts, liver-function tests, serum electrolytes, and urinalysis, repeated at weekly intervals, remained normal throughout, with the exception of serum alkaline phosphatase, which was raised to 28 K.A. units on the first estimation (before treatment started) but was normal on the next and all subsequent estimations.

Griseofulvin in divided dosage of 0.75 g. daily—that is, 15 mg./kg. body weight—was begun on April 1, 1959, and has been maintained since then. Three weeks later definite loss of fluorescence was noted in the proximal part of the hairs. After five weeks microscopical examination revealed fungus in the distal part of the hair, with a clear portion extending up to 2.5 cm. from the bulb and a fairly sharp line of demarcation (Fig. 2). Since then the clear region of the hair has continued to extend, recently at a slower rate, and the contrasting shades are now so marked as to be obvious to the naked eye (Figs. 3 and 4).

The patient's weight showed a gain of 11 lb. (5 kg.) while in hospital but returned to near its previous level before discharge. No untoward effects of treatment were noted, and she was discharged for out-patient observation after a stay of 35 days in hospital. In view of the above findings on microscopical examination and examination with Wood's light, fungistasis was considered to be complete at this stage.

CASE 2

A girl aged 12, daughter of the above patient, complained of scaling of the scalp of 10 years' duration. Confluent crusting and scarring were present over the vertex and occiput with scattered lesions on the frontal and parietal regions. Bright-green fluorescence was obtained under Wood's light. Direct microscopy revealed the presence of fungus in hairs, and *T. schoenleini* was grown in culture.

Blood counts, liver-function tests, serum electrolytes, and urinalysis, repeated at weekly intervals, remained normal throughout.

Griseofulvin in divided dosage of 0.625 g. daily—that is, 15 mg./kg. body weight—was begun on April 1, 1959, increasing to 0.75 g. on June 12 (owing to an increase in weight by 16 lb. (7.3 kg.) since her admission) and has been maintained.

Since treatment started, her progress has been similar to that in Case 1 apart from the fact that fluorescent and

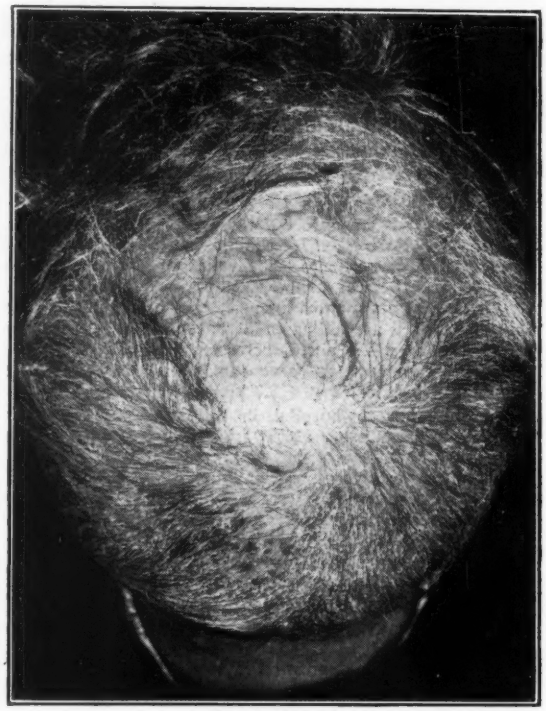

FIG. 1.—Case 1.

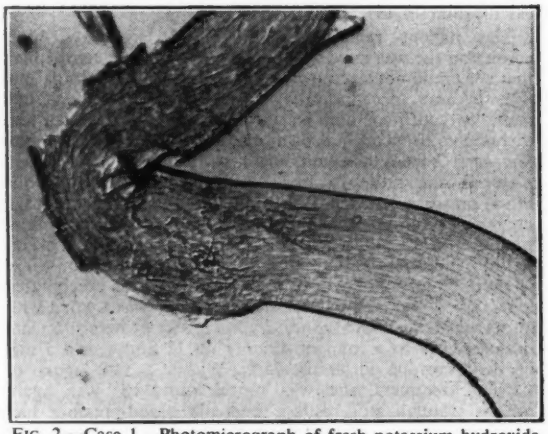

FIG. 2.—Case 1. Photomicrograph of fresh potassium hydroxide preparation of hair, showing arrest of fungal invasion of hair shaft. (×84.)

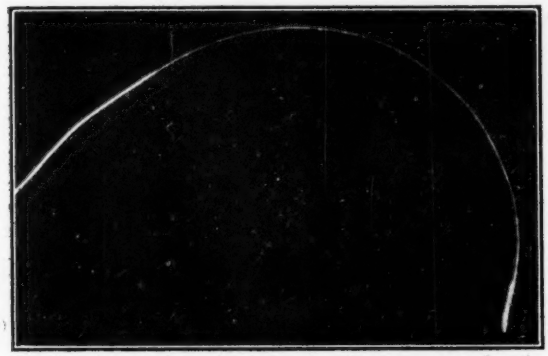

FIG. 3.—Case 1. Hair showing extent of improvement after six weeks' treatment with griseofulvin.

FIG. 4.—Same hair as in Fig. 3, showing the translucent non-infected portion of hair contrasted with the lustreless infected portion.

microscopical changes in the affected hair have been slower in development. Furthermore, in the second week of treatment she developed a mild, non-itchy, maculopapular erythematous eruption on the dorsum of both feet, with associated generalized dermographism. Treatment was continued under a cover of oral diphenhydramine hydrochloride, 200 mg. daily, and the eruption subsided. For the purposes of the present investigation she has remained under observation as an in-patient, though fungistasis was considered complete at seven weeks.

COMMENT

Our observations show that older methods of treatment of favus were unsatisfactory and prolonged, many patients defaulting before cure was certain. Any type of therapy with a promise of speedy and lasting cure, particularly if suitable for administration by injection or by mouth and devoid of toxic effects, must therefore be welcomed in the management of this disease.

The reported toxicity of griseofulvin caused us to delay systemic trial until Williams *et al.* (1958) issued a preliminary report on this aspect of its use. Gentles (1958) affirmed that low mammalian toxicity had been reported, but Paget and Walpole (1958) produced severe colchicine-like effects in rats with a dosage of 200 mg./kg. given by intravenous injection. Gentles obtained beneficial effects in *Microsporon canis* and *T. mentagrophytes* infections in guinea-pigs with doses of 60 mg./kg., and later (personal communication) with a dosage as low as 15 mg./kg. We did not know the safe limit of dosage in man, but thought that, with the possibility of long-term administration in mind, it would be of advantage if this dosage proved sufficient.

Accordingly, in spite of reports of relative resistance of *T. schoenleini* to griseofulvin *in vitro*, it was decided to use this dosage in treating the two cases described above. So far, in this dosage, it would appear that griseofulvin has succeeded in producing speedy fungistasis at least. It is not thought that the fungous organisms responsible for favus lead any other than a parasitic existence in human skin. The production of a barrier between fungus and keratin, such as is afforded by griseofulvin, would therefore seem almost certain to be followed by the death of the organism in the absence of a suitable medium for its growth. Even more than in the case of other superficial dermatophytes, *T. schoenleini*, owing to the depth to which it penetrates, would seem to be susceptible to an attack from within outwards by an agent which becomes incorporated in keratinous tissue (Gentles *et al.*, 1959), and eventual cure as distinct from simple fungistasis by administration of griseofulvin would seem a definite possibility in favus.

We thank Dr. J. C. Gentles for the photomicrograph (Fig. 2) and Mr. P. S. Waldie for co-operating in its reproduction and also for the photographs (Figs. 1, 3, and 4). Messrs. Glaxo Laboratories Ltd. kindly supplied the griseofulvin used in the trial.

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Pattern of Uric-acid Excretion During a Leukaemic Remission

In the course of an investigation into the use of uric-acid excretion for assessing white-cell turnover in leucopenia, a patient with "aleukaemic" leukaemia was observed to go into a partial remission. The changes in urinary excretion of uric acid which occurred during the remission were very remarkable, and do not appear to have been previously reported.

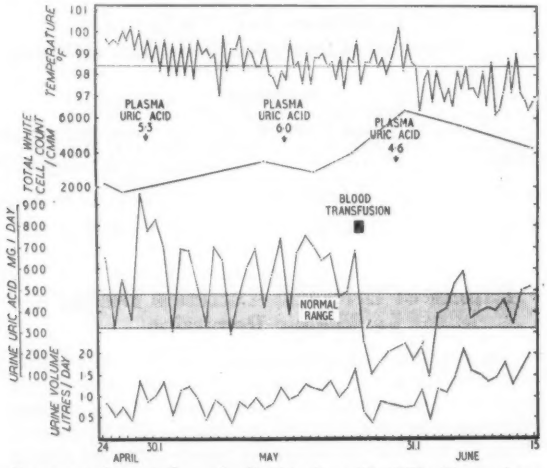
CASE HISTORY

A clerk aged 64 had a right orchidectomy for seminoma in 1952. This was followed by a full course of radiotherapy (3,600 r direct to scrotum; and 2,500 r to the anterior and 2,500 r to the posterior para-aortic glands). In February, 1958, he felt unwell, became short of breath, and was found to be anaemic. On admission to the Middlesex Hospital on April 19 he had no abnormal physical signs other than those of anaemia. His haemoglobin was 6 g./100 ml.; the film appearances were not specific. His platelets were 600,000/c.mm. and white cells 1,800/c.mm. (45% neutrophils, 46% lymphocytes, 9% monocytes). Direct Coombs test was negative. Aspiration biopsy of the marrow on April 21 showed mixed normoblastic and megaloblastic erythropoiesis, with an increase in the number of monocytes and their precursors. Free acid was present in the gastric juice.

The original diagnosis was not clear, and he was therefore given 10 mg. of folic acid twice daily by mouth, starting on April 26. His reticulocyte count rose from 2 to 9%, and the concentration of serum iron fell from 300 to 203 μg./100 ml., but there was no change in red-cell count or haemoglobin. Folic acid was continued for the next six weeks in the same dose. A transfusion of 2,500 ml. of fresh blood was started on May 24, finishing at midday on May 25. There was no reaction of any sort to this transfusion, and he felt better afterwards. Five days later his temperature settled, and remained almost normal for the ensuing month. On June 6 a second aspiration biopsy of sternal marrow showed a large increase in the number of monocytes and their precursors; and a diagnosis of monocytic leukaemia was made.

He steadily deteriorated during the following year, and suffered severely from mouth ulcers. From August, 1958, until a few days before his death in June, 1959, the peripheral white-cell count remained always under 4,000/c.mm. Primitive and abnormal mononuclears were seen periodically in the blood, and nucleated red cells also appeared occasionally. There was a consistent relative monocytosis varying between 10 and 44%. Necropsy showed widespread infiltration of liver, spleen, bone-marrow, and lymph nodes with monocytes and reticulum cells.

Excretion of Uric Acid.—The patient was asked to take a low-purine diet from the third day after his first admission (April 22) until discharge (June 15). His urine was collected into bottles containing toluene and chloroform, and was analysed for uric acid by the specific method of enzyme spectrophotometry described by Praetorius and Poulsen (1953). Continuous collections were made from 6 a.m. on April 24 to 6 a.m. on June 15. On his second admission (for blood transfusion) in August, 1958, a further short study was made, again while he was on a low-purine diet.



Sequence of events from April 24 to June 15, 1958. From above down are shown the oral temperature at 6 a.m. and 6 p.m., the total peripheral white-cell count, the urinary excretion of uric acid, and the urine volume. The three estimations of uric acid in plasma are indicated, with the values in mg./100 ml.

Results.—The Chart shows the changes in oral temperature, total peripheral white-cell count, daily urinary excretion of uric acid, and daily urine volume during his first admission in 1958. It seems clear that a partial remission took place about May 26. His total white-cell count, previously 3,000/c.mm. or less, rose to 4,000 on May 24 and to 6,500/c.mm. on June 1. On this occasion there were 47% neutrophils, 26% lymphocytes, 25% monocytes, and 2% eosinophils. Thereafter the total count fell steadily to 3,500/c.mm. on August 5, and it remained subnormal until just before death. As well as the improvement in white-cell count, there was the striking fall in temperature, and a subjective feeling of well-being. The latter may, of course, have been simply due to the relief of anaemia. The remission was incomplete, because the bone-marrow was definitely abnormal on June 6. The most dramatic change during this period occurred in uric-acid excretion. Originally this was well above the normal range (values of Crone and Lassen, 1956), but on May 26 the excretion dropped precipitously to subnormal levels, and did not enter the normal range until nine days later. Three estimations of the concentration of plasma uric acid (in mg./100 ml.) were made, and are indicated on the Chart. It is clear that the fall in excretion could not be accounted for by renal retention of uric acid. Though there was a fall in urine volume the concentration of uric acid in the urine also fell (from 50 to 20 mg./100 ml.). No other solutes were estimated, but it seems very probable that the excretion rate of several other solutes may have diminished in parallel with the fall in uric-acid excretion, and hence may have accounted for the fall in urine volume. An analogous situation may be the polyuria accompanying the reticulocyte crisis in treated pernicious anaemia (Opsahl, 1939), which is always accompanied by a high rate of uric-acid excretion.

COMMENT

It is well known that successful treatment of acute and chronic leukaemia may reduce uric-acid excretion to normal (Sandberg *et al.*, 1956), but all such observations have been made during drug treatment. The antimitotic drugs and anti-metabolites produce large temporary increases in uric-acid excretion (presumably by accelerating the rate of cell destruction), and the glucocorticoids also increase uric-acid excretion (probably mainly by their well-known effect in increasing renal urate clearance). In the present case no such drugs were given, and the pattern of a remission could therefore be clearly seen.

The use of urinary excretion of uric acid as a measure of the rate of destruction of blood cells requires certain assumptions, which have been discussed by Sandberg *et al.* (1956). Blood transfusion itself has little effect, according to Opsahl (1939); and I have confirmed this on several occasions. The dramatic fall in uric-acid excretion during the remission in this patient strongly suggests that a previously high rate of cell destruction suddenly ceased, and that for nine days it remained subnormal. It is interesting to consider whether the normal or the leukaemic cells, or both, were originally being destroyed at an increased rate. Since the total counts of neutrophils, lymphocytes, and monocytes all increased during the remission it seems most probable that the high rate of destruction affected normal cells. Kaplan and Smithers (1959) have suggested a similar mechanism in the malignant lymphomas. Though there is much present dispute about the estimates of white-cell life-span made by the ^{32}P deoxyribonucleic acid labelling technique (Perry *et al.*, 1958), it can be said that most observers put the life-span of normal granulocytes at about nine days, which would fit well with the observed pattern of uric-acid excretion in this patient.

Most of the difficulties in interpreting cross-transfusion and inoculation experiments in human and experimental leukaemia are resolved by the general conception that the fundamental abnormality in leukaemia is the presence of an abnormal clone of cells arising by somatic mutations (Burnet, 1959). Particularly in the early stages, there will be a delicate balance between the abnormal and the normal cell population. Since both circulating and non-circulating anti-leucocyte antibodies can often be demonstrated in acute leukaemias (Bernard *et al.*, 1954), it is possible that the final inevitable success of the leukaemic population might in some cases be accelerated by an increased rate of destruction of normal white cells. If the abnormal cells are of mesenchymal origin, as they are in leukaemia, they may retain the capacity of forming antibodies; and, being of a different genetic structure, they may form auto-antibodies against normal white cells. Since the products of white-cell breakdown are generally believed to play some part in stimulating the marrow to produce more white cells, this stimulation, affecting leukaemic as well as normal cells, will then complete a vicious circle which may well enormously accelerate the progress of a leukaemia.

It is not at all clear what happens in a remission. The remission in this patient may have been induced by the fresh blood transfusion, though the white-cell count

had started to rise just before the transfusion. The effects on uric-acid excretion were certainly not the effects of the blood transfusion *per se*, since control observations were made on this same patient on the three days following his second transfusion (also of 2,500 ml. of fresh blood) in August, 1958. On this occasion the uric-acid excretion on the three days after transfusion was 573, 548, and 715 mg./24 hours—that is, a greatly increased amount, sharply contrasted with the abrupt fall after the first transfusion (illustrated in the Chart).

Further work is needed, particularly since there may be fallacies in relying on the results of uric-acid studies. It is remotely possible, for example, that accelerated uricolysis (Bien *et al.*, 1956) could entirely explain the observations made in this patient. However, this would entail a rate of uricolysis exceeding 60% of the normal daily production—a rate which has not yet been shown to occur in human beings. The simplest explanation is that acute reduction in the rate of normal white-cell destruction was the first event, which, by tilting the balance in favour of the normal cell population, produced a temporary clinical and haematological remission.

I am grateful to Professor A. Kekwick and Dr. Deborah Doniach for helpful criticism. I am indebted to the Clinical Research Committee for facilities provided in the Institute of Clinical Research, Middlesex Hospital Medical School, London.

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Hypotension Due to Meprobamate Overdose

Attention has been drawn to the dangers of meprobamate (*Brit. med. J.*, 1958). The following case of meprobamate overdosage is thought to have some features of interest.

CASE REPORT

A 19-year-old Swedish girl, employed as a resident maid in a children's home, shared a room with another girl and was not noticed to have been depressed or to have been behaving abnormally until at 6.30 a.m. on the day of admission an unsuccessful attempt was made to awaken her. At 8.15 a.m. a doctor was called as she was still unrousable. She was unconscious, with stertorous breathing. The pupils were dilated but reacted to light, and the corneal reflexes were present, as were the tendon jerks. The plantar reactions were down-going. The muscles were flaccid.

At 9.45 a.m. the patient was admitted to hospital, where the original findings were confirmed. The blood-pressure was 100/60, the pulse 70, and the temperature 96.6° F. (35.9° C.). She could be roused by loud speech, when she would open her eyes briefly and look around her. She would also react in a purposive manner to unpleasant stimuli such as pin-prick or plantar stimulation, and would try to cover herself with the bedclothes when these were removed during examination. Though her muscular tone was low, power appeared to be fairly good. She was given 2 ml. of nikethamide intravenously and her stomach washed out. No tablets were recovered. Gastric washings and urine were negative to tests for barbiturate and aspirin derivatives.

One hour after admission the blood-pressure had dropped to 90 systolic, and at two hours it was 80 systolic. No further change in the level of consciousness had occurred; the pulse was 80 and weak. She showed no evidence of shock. Her general appearance gave no idea of her falling blood-pressure. She was not cyanosed and her skin was warm.

Three hours after admission the blood-pressure was 60 systolic and the pulse was becoming difficult to feel. At this time no tablets had been discovered, and as the clinical picture did not fit barbiturate or aspirin poisoning a lumbar puncture was done, the findings being normal. She was still conscious enough to object to this procedure by moving her limbs. It was decided to treat the hypotension symptomatically, and while a drip trolley was being prepared the blood-pressure became unrecordable. There was no change in respiration. Mephentermine sulphate, 30 mg., was given intravenously; the blood-pressure rose at once to 80 systolic, falling during the next 15 minutes to 60 systolic, when an intravenous infusion of 4 ml. of L-noradrenaline in a pint (570 ml.) of glucose-saline was begun. The blood-pressure responded at once, being readily controlled and maintained between 100 and 120 systolic.

The patient's consciousness gradually returned, so that six hours after admission to hospital her eyes were open and she was able to say that she felt better. At about this time a box containing 70 whole 200-mg. tablets of meprobamate and some broken fragments was brought to the ward, having been found among her belongings. She admitted taking some of her tablets the previous evening, but would not state how many or what her consumption of tablets had been over the period immediately prior to her illness.

The patient's mother arrived from Sweden 24 hours after the patient's admission and gave the history that her daughter was "nervous" and had taken overdoses of the same tablets in January, 1957, and February, 1958. She had not been treated in hospital on either occasion. The tablets in her possession were the remainder of 200 sent her from Sweden three months previously. A sister aged 22 years had received insulin-coma treatment and electric convulsion therapy.

Eleven hours after her admission noradrenaline was omitted from the drip without further disturbance of blood-pressure, which remained at about 120/70. The patient was fully ambulant 36 hours after admission, and was discharged home to Sweden on the fifth day after admission. Up to this time no sequelae had been noted.

COMMENT

In this case of meprobamate overdose the fall in blood-pressure was out of proportion to the depression of consciousness. The occurrence of hypotension is described in most of the 17 or so other cases reported (Shane and Hirsch, 1956; Heberden and Cooper, 1957; Powell *et al.*, 1958; Bedson, 1959). The patient's general condition gave little indication of her falling blood-pressure; the symptom responded readily to mephentermine and noradrenaline.

I thank Dr. Philip H. Willcox for his kindness in allowing me to report his case.

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Reviews

DISEASES OF THE SPINE

Modern Trends in Diseases of the Vertebral Column. Edited by Reginald Nassim, B.M., F.R.C.P., and H. Jackson Burrows, M.D., F.R.C.S., F.R.A.C.S. (Pp. 292+ix+11; illustrated. 75s.) London: Butterworth and Co. (Publishers) Ltd. 1959.

This book is interesting, informative, and an outstanding addition to surgical literature. There are 15 contributors, each writing on a subject to which he has added knowledge during the last 20 years. The articles are well chosen, and the subjects of more than half bristle with difficulties. The anatomy and development of the spine (Walmsley) are concisely described, so as to be helpful to the surgeon. This subject might have been followed with advantage by the article on radiology (Carstairs), for the text and figures of this should be studied before the other chapters are read. Congenital abnormalities (Harris of Toronto) and structural scoliosis (J. I. P. James) are monographs of note. Harris describes clearly the many types of anomaly he has seen, and brings to our notice the neurological symptoms that may be associated with them. Spondylolisthesis—Newman also writes on this—and diastematomyelia are ably described, but many aspects of spina bifida are neglected. The contribution of James is particularly valuable because of his studies of prognosis, and his remarks on treatment makes it possible to appreciate the thought that has been given to improving conservative treatment and to the selection of patients for operation. That surgeons and neurologists have had considerable experience of cervical spondylosis (Logue) is well shown by the lucid description of the condition, but the discussion of the differential diagnosis from conditions below the intervertebral foramina is limited. The paragraphs on the anatomy of the nerve root and root-sleeve fibrosis are excellent.

Both physicians and pathologists make useful contributions to the textbook; osteoporosis is covered by Nassim, and degenerative diseases by Collins, who includes pathological conditions of the intervertebral disk in his article. Tumours are dealt with by Sissons. This difficult subject made it necessary to include the work of others with his own experience. The order in which he considers it is unusual and somewhat confusing. Fortunately, tumours are rare, but it would have been interesting to be given information on tumours of pedicles and vertebral arches, with reference to pressure on the cord, and their prognosis, and also on tumours affecting the sacrum. Hart has been reporting observations on ankylosing spondylitis for some years, and in this textbook he describes the character of the disease and stresses the necessity for a period of observation before arriving at the diagnosis. Tegner discusses symptoms relating to the back of organic and psychogenic origin, and writes on the management of the latter.

The illustrations are well chosen and of high quality, especially in the chapter on degenerative diseases. Although radiographs of the spine are often not suitable for reproduction, those in Carstairs's chapter reach a remarkably high standard. The editors are to be congratulated on this volume, and it is hoped that the surgical editor will make a direct contribution when a subsequent edition is published.

ST. J. D. BUXTON.

A MAJOR TEXTBOOK ON NUTRITION

Human Nutrition and Dietetics. By Sir Stanley Davidson, B.A.Cantab., M.D., F.R.C.P.Ed., F.R.C.P.Lond., M.D. Oslo., A. P. Meiklejohn, M.A., B.Sc., D.M.Oxon., M.R.C.P. Lond., and R. Passmore, M.A., D.M.Oxon. Foreword by Lord Boyd Orr, D.S.O., *M.C.*, LL.D., F.R.S. (Pp. 844+xii; illustrated. 84s.) Edinburgh, London: E. and S. Livingstone, Ltd. 1959.

This is one of the most important books to be reviewed in these columns for some time, and must be regarded as a major addition to textbooks of medical science. It is beautifully written and the text gives no hint of the triple authorship. It is not only a book of great scholarship, but it is also extremely readable and it contains some apt quotations. It was particularly delightful to read Homer's comparison of the impatient Odysseus with a man roasting a sausage in front of a hot fire.

The book is divided into six parts. Part I gives an account of the physiology of nutrition, reminding us, among other things, that the spontaneous regulation of food intake was not designed to cope with the mechanized sedentary conditions of modern life. The second part gives a description of the foods commonly eaten by mankind. Many of us will wish that our mothers could have read the section on sago, tapioca, and arrowroot, and learned that these foods are almost devoid of proteins, minerals, and vitamins. Part III deals with the primary nutritional diseases, and Part IV with the nutritional aspects and dietetic treatment of general diseases. Part V deals with the public-health aspects of nutrition, and contains a series of valuable chapters on subjects such as nutrition surveys, the population problem, famine, and so forth. The final part deals with diet in conditions of physiological stress, such as pregnancy, lactation, and childhood; athletics; and climatic extremes.

The science of nutrition is still full of controversy, but subjects such as the modern loaf, fats, and essential fatty acids in the diet are handled in a balanced way, while the authors are justifiably iconoclastic in dealing with the nutritional neuropathies. The immense difficulties in feeding the inflated world population, in changing food habits, in overcoming custom and religious taboo, and in preventing the continuous degradation of the soil by over-exploitation, wars, and neglect are properly displayed. Handling this large volume of 844 pages, the educationist cannot help wondering where precisely the study of human nutrition and dietetics should come in the curriculum. At present, as the authors say, it is given only a small place, and is uneasily divided between the departments of biochemistry, physiology, clinical medicine, and public health. Most of my generation learnt these subjects after qualification, and I can remember long hours spent poring over Abderhalden and Graham Lusk. For the undergraduate this can only be a reference book, but the candidate for the M.R.C.P., F.R.C.S., D.P.H., or D.T.M. would be better employed in reading it from cover to cover than in chasing the ephemeras of the current literature.

L. J. WITTS.

SKIN SENSE

Practical Dermatology. By George M. Lewis, M.D., F.A.C.P. (Pp. 363+xv; illustrated. 56s.) Philadelphia and London: W. B. Saunders Company. 1959.

Dr. George Lewis is a sound clinician with great experience, and a teacher who is held in high regard. He is also learned in the scientific branches of his

subject and an authority on mycology. His textbook on practical dermatology, of which this is the second edition, is all the more remarkable for its simplicity and for presenting the essentials of the subject for student and general practitioner. The field of the common dermatoses is fully covered, the descriptions of clinical features are brief but adequate and clear. There is no waste of words on theoretical speculations, and aetiology is dealt with in a realistic fashion. Treatment similarly is clear and limited to common practice.

Though the author's experience is related to American practice, he tackles his subject in much the same way as do his British colleagues. There is an abundance of common sense and of general medicine in his approach and teaching, blended with the distinctive and particular features of dermatological practice. There are some valuable chapters at the end of the book linking skin affections with those of other organs and indicating those dermatoses which suggest general ills. Pemphigus, which has figured largely in recent British literature, is not mentioned, or dithranol in the treatment of psoriasis. We would probably emphasize the spontaneous disappearance of cavernous angiomata and of lichen planus more than the American schools, and would doubt the necessity of gastric analysis in rosacea or of the administration of arsenic in any chronic dermatitis. But it is difficult to do other than praise this crisp presentation of the subject in an attractive small volume, admirably illustrated and of reasonable price.

J. T. INGRAM.

PORTAL HYPERTENSION

Bleeding Esophageal Varices. Portal Hypertension. By Hirsch Robert Liebowitz, B.S., M.D. Section on Surgical Treatment in collaboration with Louis M. Rousselot, M.D., M.S.(Surg.), Med.Sc.D.(Surg.), F.A.C.S. Foreword by Allen O. Whipple, M.D., F.A.C.S. (Pp. 986+xxxiii; illustrated. £9 3s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

This is the most complete book on portal hypertension yet published, and is in fact a survey of most of the literature on this subject. The author started with the necropsy material of 50 cases of ruptured varices at the Bellevue Hospital, New York, and has expanded this with the help of Dr. Rousselot into this almost 1,000-page volume. After chapters on the vascular anatomy of the liver and the haemodynamics of the portal circulation, the author considers the effect of gross haemorrhage on this circulation. The methods of recording portal pressures are then surveyed, and this is followed by an account of the pathological conditions which give rise to portal hypertension. There is an excellent chapter giving up-to-date views on portal-systemic encephalopathy, and the book finishes with two chapters on the surgical management of these cases by Dr. Rousselot, who was the first person to record the portal pressure in man and has had a long experience of the management of these cases. Particular prominence is given to the treatment by portacaval anastomosis, but the difficult problem of the management of patients in whom this type of operation is impossible is rather glossed over.

This book will for a long time prove to be a very useful work of reference for those interested in this subject, but the general worker may have some difficulty in finding what he wants among the mass of detail which is given here. It is a very well presented volume and should be in every medical library.

R. MILNES WALKER.

CANCER IN NORWAY

Cancer Registration in Norway. The Incidence of Cancer in Norway, 1953–1954. By Einar Pedersen and Knut Magnus. Foreword by Fredrik Mellbye. (Pp. 183.) Oslo: Landsforeningen mot Kreft (The Norwegian Cancer Society). 1959.

The Norwegian Cancer Registry is a joint project of the Ministry of Social Affairs, the Central Bureau of Statistics, the Norwegian Radium Hospital, and the Norwegian Cancer Society, and this report—the Registry's first major publication—covers the two-year period 1953–54. No account is given of the treatment of cancer, but it is planned that the survival studies, now under way, should throw light on this subject in later publications. The present publication is in English to meet the needs of the many foreign research workers interested in these Norwegian studies.

During 1953 cancer was diagnosed in 7,684 males and 8,044 females, and these figures were nearly 50% higher than those for deaths from cancer in the same period. In the chapter on the incidence of cancer by individual sites some rather curious figures are given with regard to the lips: cancer in this site was many times more frequent in males than in females, but this was true only of the lower lip, with 223 male and only nine female cases, whereas there were six male and five female cases of cancer of the upper lip. The relative liability of males to develop cancer of the respiratory tract, of which there were 679 new cases, was such that 6.4% of all the male cases and only 2.3% of all the female cases were thus located. The sparingness with which the authors of this report have ventured to speculate over the possible explanations of these sex differences in the incidence of cancer bears witness to their respect for the pitfalls lying in wait for the unwary statistician. Approximately half of this report is devoted to tables giving data concerned with the distribution of the cases of cancer according to sex, site, district (urban or rural), age, etc. These cases are also classified according to whether they were or were not histologically confirmed.

CLAUDE LILLINGSTON.

CLINICAL PSYCHOPATHOLOGY

Klinische Psychopathologie. By Kurt Schneider. Fifth edition. (Pp. 166+viii. DM. 12.80.) Stuttgart: Georg Thieme Verlag. 1959.

This book is concerned with those aspects of abnormal psychology which are of importance for psychiatric nosology. The author has been strongly influenced by Jaspers. The presentation is condensed and dogmatic. The concept of mental disease is "strictly medical"—that is, mental diseases are physical diseases. The so-called endogenous psychoses are included because they are assumed to be of organic origin. All other mental disorders without known organic pathology are "abnormal variants of psychic disposition." There are no neuroses, only neurotics. It is hardly ever difficult to decide whether a patient is suffering from a psychosis or whether he is "psychopathic." These are some of the statements made by the author, who admits that quite a few of them rest on faith rather than on evidence. Schneider's concept of psychopathic personalities as "abnormal personalities who either suffer personally because of their abnormalities or make the community suffer because of them" must be one of the most elegant but also one of the most question-begging definitions in the whole of psychiatry. It includes the neurotics.

The author has thought and written a great deal about the nature of delusion. He has attempted to trace the

steps of the delusional mental process. He also proposes a new classification of depressions. The possibility that a symptom may have a symbolic meaning is not considered. Psychogenic pain, therefore, is regarded as based on "real pain"—that is, on an organic cause. The weakest part of the book is the appendix, in which the author presents an introduction to the abnormal psychology of feelings and instincts. A doctrine of abnormal psychology which refers neither to experimental psychology, nor to neurology and neurophysiology, nor to psycho-analysis, but leans heavily on philosophy, is an anachronism. The author is at his best when he discusses clinical diagnosis, and here some of his statements can be tested. The experienced and discriminating psychiatrist will find the book interesting. Although he may frequently disagree with the author, he will be stimulated into re-examining his own concepts.

E. STENGEL.

WOMANHOOD

Womanhood. By Margaret Moore White, M.D., F.R.C.S., F.R.C.O.G. Foreword by Professor W. C. W. Nixon. Illustrations by Dr. Mary D. G. Jones. (Pp. 144. 10s.) London: Delisle. 1959.

This new edition of Miss Margaret Moore White's book has been enlarged and completely revised. It seeks to trace the progress of woman from puberty through marriage, childbirth, and to the menopause. There are, in addition, chapters on gynaecological disorders and operations.

Presumably this book is intended for the intelligent lay woman; it is certainly too superficial in its approach to appeal to doctors or nurses. Its chief merits are the clear and concise way in which the subjects are dealt with, and the accuracy of its information. As an introduction to the subject and as an authoritative account of matters which many women worry about and find difficult to understand, it can be recommended. Most readers, however, who are looking for information on a single topic such as birth control, will want more detailed information, and a fuller bibliography could have been included with advantage.

This book can be recommended as a brief but useful addition to the literature of health education.

JOSEPHINE BARNES.

Almost any systematic investigation in medicine, whether at the bedside or at the laboratory bench, produces data suitable (and all the better) for statistical analysis. If the investigation has been planned from the beginning with that in mind, the analysis is likely to be more informative. Two books on this kind of planning are *Experimental Design in Psychology and the Medical Sciences*, by A. E. Maxwell (Methuen, pp. 147, 17s. 6d.), and *Planning of Experiments*, by D. R. Cox (John Wiley, pp. vii+308, 60s.). Dr. Maxwell's is the more concise and summary of the two, Dr. Cox's the more thorough and extensive. Both begin with the elements of their subject and neither requires the reader to be an expert mathematician. Dr. Maxwell gives a clear account of statistical tests and then takes the reader through various ways of arranging experimental investigations so that the most information may be extracted from them. Dr. Cox discusses not only the techniques of experimental design but also many of the ideas underlying them. A book that concentrates more on statistical testing and less on design is *Statistical Methods in Biology*, by N. T. J. Bailey (English Universities Press, pp. ix+200, 25s.). This book also starts from the elements and gives a clear account of statistical techniques without bothering much about the theory underlying them. It should be helpful to medical readers.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Principles of Human Pathology. By Edward B. Smith, M.D., Parker R. Beamer, Ph.D., M.D., Frank Vellios, M.D., and Dale M. Schulz, M.S., M.D. (Pp. 1,123+xi; illustrated. 95s.) New York and London: Oxford University Press. 1959.

Chronic Illness in the United States. Volume III. ***Chronic Illness in a Rural Area. The Hunterdon Study.*** Reported by Ray E. Trussell, M.D., M.P.H., and Jack Elinson, Ph.D. (Pp. 440+xiv. 60s.) Cambridge, Mass.: Harvard University Press (Commonwealth Fund). London: Oxford University Press. 1959.

Public Health in the Town of Boston, 1630-1822. By John B. Blake. (Pp. 278+x; illustrated. 52s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1959.

Medical Helminthology. By J. M. Watson. (Pp. 500; illustrated. 84s.) London: Baillière, Tindall, and Cox, Ltd. 1960.

Klinische Chirurgie für die Praxis. Edited by Professor Dr. O. Diebold, Professor Dr. H. Junghanns, and Professor Dr. L. Zukschwerdt. In four volumes. Volume I, Part 2. (Pp. 144; illustrated. DM. 27.) Stuttgart: Georg Thieme Verlag. 1960.

Nebenschilddrüseninsuffizienz und Tetanisches Syndrom. By Professor Dr. Jochen Quandt and Dr. Werner Ponsold. (Pp. 176+viii; illustrated. DM. 17.80.) Jena: VEB Gustav Fischer Verlag. 1959.

Einrichtung und Methoden des Klinischen Laboratoriums. By Dr. Eberhard Goetze. (Pp. 246+x; illustrated. DM. 21.90.) Jena: VEB Gustav Fischer Verlag. 1959.

The Aetiology and Arrest of Pre-Eclamptic Toxaemia with Early Ambulant Treatment. By K. Douglas Salzmann, M.D., M.R.C.P.(Ed.), D.Obst.R.C.O.G. (Pp. 69+viii. 10s. 6d.) London: H. K. Lewis and Co., Ltd. 1960.

Surgical Note-Taking. A Booklet for Surgical Dressers and Clerks Commencing Clinical Studies. By Charles F. M. Saint, C.B.E., M.D., M.S., F.R.C.S.(Eng.), F.R.A.C.S.(Hon.), and Jan H. Louw, Ch.M. Fifth edition. (Pp. 172+viii. 12s. 6d.) London: H. K. Lewis and Co., Ltd. 1960.

The Surgeon's Log. By J. Johnston Abraham. Seventh edition. (Pp. 244+xii; illustrated. 18s.) London, Melbourne, Toronto: Heinemann. 1959.

Outline of Orthopaedics. By John Crawford Adams, M.D. (Lond.), F.R.C.S.(Eng.). Third edition. (Pp. 440+vii; illustrated. 35s.) Edinburgh and London: E. and S. Livingstone, Ltd. 1960.

The Roots of Crime. By Edward Glover, M.D., LL.D. ***Selected Papers on Psycho-Analysis,*** Volume II. (Pp. 422+xiii. 45s.) London: Imago Publishing Co., Ltd. 1960.

Électrocardiographie Clinique. Théorie et Pratique. By Enrique Cabrera. Translated by Dr. Jean Laham. (Pp. 260; illustrated.) Paris: Masson et Cie. 1959.

Annuario Statistico 1953-1958. Istituto Nazionale per l'Assicurazione Contro le Malattie Servizio Statistico-Attuariale. (Pp. 347.) Rome: Tipografia U. Quintily. 1959.

Malformations Congénitales du Cerveau. By G. Heuyer, M. Feld, and J. Gruner, with 26 contributors. (Pp. 450; illustrated.) Paris: Masson et Cie. 1959.

Ophthalmic Nursing. By J. B. Foster, M.A.(Cantab.), M.B., B.S., D.O.(Melb.), D.O.M.S.(Lond.), F.R.C.S., F.R.A.C.S. (Pp. 134+x; illustrated. 21s.) London: Angus and Robertson. 1959.

A Hundred Years of District Nursing. By Mary Stocks. (Pp. 229; illustrated. 25s.) London: George Allen and Unwin, Ltd. 1960.

Consequences of Disturbance. The Pest Situation Examined. By Alan Mozley, D.Sc., Ph.D., F.R.S.E. (Pp. 61+x. 9s.) London: H. K. Lewis and Co., Ltd. 1960.

Variations on a Theme by Sydenham: Smallpox. By P. B. Wilkinson, M.R.C.P. (Pp. 76; illustrated. 17s. 6d.) Bristol: John Wright and Sons, Ltd. 1959.

The Microcirculation. Symposium on Factors Influencing Exchange of Substances Across Capillary Wall. Edited by S. R. M. Reynolds and Benjamin W. Zweifach. (Pp. 170+viii; illustrated. $4.50.) Urbana: University of Illinois Press. 1959.

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ERADICATION OF MALARIA

The first proposals for national, continental, or even larger projects for the eradication of malaria came rather suddenly at the Eighth World Health Assembly in 1955, and had the appearance of being inadequately prepared and perhaps supported by arguments which might have been more logically used in another cause—the encouragement of research into resistance to insecticides. However, malaria eradication soon outlived this slightly inauspicious start and the World Health Organization has chosen as the theme for World Health Day, on April 7, "Malaria Eradication—a World Challenge." Both natural and human influences have played a part in banishing malaria from some parts of the world. It disappeared spontaneously from much of Europe and North America ; and it was evicted successively from Cyprus and Sardinia and Chile in schemes which represented the last of the old methods, based primarily on control of breeding. The new methods of exclusive reliance on residual insecticides unexpectedly resulted in its eradication from Crete, parts of Greece, Italy, British Guiana, Venezuela, and some other places, while in the U.S.A. a deliberate eradication scheme based on the concept that malaria was diminishing and that its disappearance could be expedited proved successful. A standard framework on which individual national schemes should be built was worked out[1] and found usable ; no more than minor adjustments were needed when it was later reviewed.[2] The scale of the task was estimated, first by P. F. Russell,[3] and later by the World Health Organization, and was found to entail the protection of 1,260m. people in member States of W.H.O., and about 200m. people elsewhere, chiefly in China.

It was perhaps the very magnitude and ambition of the idea which attracted the abundant enthusiasm, technical aid, and financial and material support which led to the wide application of eradication schemes. Financed principally by the countries concerned, they were supported by technical help from W.H.O. Other international organizations such as U.N.I.C.E.F. gave material aid, as did the U.S.A. It was reported to the Twelfth World Health Assembly in 1959 that the population of areas in which eradication had already been achieved amounted to 283m., while current campaigns were affecting 772m. others.

The encouragement given by these figures was immense, though the reports made it clear that the successes included those achieved before the deliberate adoption of eradication as an international policy, and that more than nine-tenths of the current campaigns were still in too early a stage for the assessment of results. Nevertheless, progress had so far been most satisfactory. Broadly speaking, malaria had disappeared from most of southern Europe and the Mediterranean islands, almost entirely from the Russias, from large parts of South America, from the U.S.A., and from some relatively small areas in Asia and the southernmost part of Africa. The schemes then under way covered all the remaining countries of the Americas and Europe which were in the malaria belt, most of the malarious territories on the mainland of Asia except Malaya, Cambodia, and, at that time, Pakistan, and plans were in hand for the Middle Eastern countries and the East Indian islands.

Success has so far lain chiefly in the Americas and in Europe, in which the populations at risk constitute only 34% of the total in the member States: in Asia, the home of almost half of those at risk, success is still very restricted. There is as yet no single large example of eradication in Africa and there are not even any plans for the eradication of malaria in the greater part of the equatorial African area in which transmission is unusually severe.

Is the order in which eradication schemes are progressing the start of a steady series of successes to follow the earlier ones, or is it to any noticeable extent a division into success and failure? There is certainly enough evidence of difficulty to justify very careful stocktaking. Malaria eradication is a world challenge, but to what? To continue steady support on existing lines? To increase the intensity of effort? To modify techniques? To withdraw from large areas, as at least one international body which finances eradication has suggested? To initiate or intensify some forms of research? These are live questions which demand more critical examination than they have yet received in public, and without

[1] *Wld Hlth Org. techn. Rep. Ser.*, No. 123. Expert Committee on Malaria, Sixth Report, 1957. Geneva.
[2] Ibid., No. 162. Expert Committee on Malaria, Seventh Report, 1959. Geneva.
[3] Russell, P. F., *Amer. J. trop. Med. Hyg.*, 1956, **5**, 937.
[4] Bruce-Chwatt, L. J., *Bull. Wld Hlth Org.*, 1959, **21**, 737.

which they must remain largely in the air, unanswered.

The process of eradication includes two main activities: the complete and locally ubiquitous prevention of transmission by a well-drilled insecticidal practice continued for four or more years, and a system called surveillance which starts towards the end of this time and includes case-finding, treatment, and epidemiological study aimed at the identification and elimination of residual foci or other sources of reinfection.

The attack on mosquitoes rests on a sound experimental basis, but such details as dose and cycle of treatment are largely empirical and may often be dependent on budget estimates and the ordering of supplies years beforehand. Yet the routine process of insecticidal attack needs a very high standard of technical control and much flexibility of administration and supply if it is to be universally successful.

Surveillance also needs a most imaginative approach of a type which is new to most malariologists. Success depends on the vigorous search for evidence of failure, and the utilization of discovered cases or other possible sources of evidence as clues which might lead not only to a single remaining focus of the disease but also to a demonstration of the type of place in which other small foci might be found.

If all goes well with measures applied in this way a routine can be followed and eradication can eventually be claimed. Lack of success in achieving eradication has often been matched by intensification of efforts and by suggested reasons for partial failure. The published records, however, contain too few detailed studies of the anatomy of failure, of its homogeneous or irregular dispersion in space and time, to enable the investigator to go to the actual spot where transmission occurs, at the time when it happens, and thus give him an opportunity to be precise in his statement of cause and remedy.

The difficulty created by anopheline resistance to insecticides has not disappeared: resistance has grown more widespread, but the threat has certainly grown less ominous in the light of research carried out since 1955. There is good reason to think that steady progress in the successful eradication of malaria might be assured if the basic principles of epidemiological study could be brought effectively to bear at all stages of eradication campaigns, particularly when they lag. They need continued financial support, but there is nothing which attracts it so much as the exhibition of technical competence, and the real challenge of malaria eradication so far as it concerns the medical world is to ensure this.

MORE DYSENTERY

One of the epidemiological features of dysentery in Great Britain is that the incidence of it usually rises to a peak at about this time of year. The graph in our Vital Statistics section (p. 1065) shows that it is at present running true to form. The size of the epidemic varies from year to year. This year the weekly notifications are at about the same level as in 1956, when the largest recorded epidemic occurred.

The overwhelming majority of these cases are due to *Shigella sonnei*, other varieties of dysentery accounting for less than 5% of the total. Mortality is very low. In 1956 there were 33 deaths among nearly 50,000 notifications. But probably only a minority of the persons infected during an epidemic are detected, for the classical symptoms of dysentery are frequently absent. The infection in many cases is symptomless or marked by a trifling attack of diarrhoea for which medical advice is not sought. Herein lies one of the difficulties in control of the disease. Sometimes local publicity, resulting perhaps from an outbreak in a school, may heighten public awareness of the disease and temporarily increase the proportion of cases brought to light. The diagnosis is confirmed bacteriologically in a considerable number of those cases that are notified, but many unconfirmed cases are probably not notified; some may be notified as food-poisoning.

Food-borne outbreaks of dysentery are less common in Great Britain than they were, and the autumn epidemic peak formerly seen and probably due to infection from food has now disappeared. The principal methods of spread are direct and indirect personal contact. Outbreaks have always been common in day-nurseries, and appear to be occurring more frequently nowadays in schools. In both these situations it is common to find that many of the contacts have become infected by the time the presence of the disease is recognized. Infected children take the infection back to their families. On the introduction of the disease into a family over two-thirds of the children and about a fifth of the adults may expect to become infected. When the disease is prevalent in a district it is almost certain to be introduced into the local school, and unless the utmost vigilance is exercised it will be further disseminated from there into the community.

Why epidemics occur at this time of the year is not certain, though low temperature and high humidity favour the survival of *Shigella sonnei* outside the body. This may assist transmission of infection by lavatory seats, plug handles, door knobs, and so on. The infective dose appears to be

very small, a factor that would allow wide spread during epidemics.

Control of the disease presents many difficulties. No single method can be relied on, and a concerted attack on all fronts is necessary. There must be a thorough search for infected persons, who, once discovered, should be promptly treated. In centres of infection, such as schools, additional precautions may be needed during an epidemic, including special arrangements for cleaning and disinfecting the lavatory. It may be necessary, for instance, to organize supervision of the hand-washing routine. Where roller towels are used the temporary substitution of paper towels may be helpful, and some authorities recommend that all children should regularly dip their hands in a bowl of a quaternary ammonium disinfectant.

Since many infected persons have no symptoms, bacteriological examination of contacts is the only way of finding out how widely the infection has spread. Repeated surveys of school classes can be a large undertaking, and the disease is often not controlled by them. It is no use examining school contacts unless home contacts are examined at the same time, for reinfection can take place at home. The best results are obtained when the bacteriological survey, and increased attention to case-finding and hygiene, are applied at the first appearance of trouble before the disease has had the chance to spread widely. When an epidemic threatens, all concerned should be on the look-out for the first signs of dysentery in nurseries, schools, hospitals, and old persons' homes, for once the disease has spread in an establishment it may prove very difficult to eradicate.

CONTROL OF INFLUENZA

Virologists have for many years believed that when pandemics of influenza occur the strain of virus responsible is so different from its predecessors in antigenic constitution that the immunity built up against them is ineffective against the new strain. A new report[1] from the Ministry of Health describes the epidemic Asian influenza (A2) in Britain. This was the first pandemic to be intensively studied throughout the world by modern methods, and records of it might teach us how to control a pandemic if one occurs again.

The virus was isolated in South West China in February and recognized to be of a novel antigenic type. It was tracked by a chain of laboratories as it spread across the Far East and round the World. After being isolated in Singapore in April, it was flown to Britain, rapidly checked at the World Influenza Centre, and passed on to vaccine manufacturers, who made and distributed as much as they could of a formalin-inactivated vaccine. The vaccine was not completely effective, but one, or, better, two, injections gave substantial protection to the small numbers who received them before the epidemic began. The report indicates that much more vaccine might have been prepared in Britain before the arrival of the epidemic if the news of the epidemic and the virus had been promptly sent here from Peking. If it had been sent it might have been possible to protect most key workers, for example, in hospitals, transport, and postal services, and so reduce the disruption of daily life. More persons might have been protected if a live vaccine could have been used : the virus from one egg might then have protected dozens or hundreds of persons instead of only a few. However, though live vaccine was widely given in the U.S.S.R. and seemed to be effective there, most small-scale trials of the method in other countries have been unsuccessful. Clearly improvements in reporting, in distribution of epidemic strains of virus, and in techniques of vaccination are desirable.

Quarantine is successfully combined with vaccination in the control of smallpox, but is much more difficult to apply in stopping the spread of influenza. By closing its frontiers during a pandemic a nation could probably keep out infection for the time being, but such action would cause more disruption than an ordinary epidemic—and even with extensive vaccination the epidemic would probably follow in the end. The report advises that patients with the disease should be isolated, usually at home. This might have little effect on the spread of the virus through the community, though with careful nursing it should help to reduce the risk of complications developing. At any rate the individual would probably cut down his chance of being infected if he avoided crowded places and reduced personal contacts during an epidemic. If these recommendations sound rather undramatic, they may nevertheless be more effective than seems likely at first sight. It is of interest, for instance, that at a recent international meeting[2] at least one expert argued that the Asian pandemic virus was not much less virulent than earlier pandemic strains. The relative mildness of the recent pandemic was attributed to the rarity of fatal bacterial infections—perhaps a result of improved hygiene, modern chemotherapy, and some luck.

[1] *The Influenza Epidemic in England and Wales, 1957-1958.* Reports on Public Health and Medical Subjects, No. 100; 1960. H.M.S.O. (4s. 6d.).
[2] *Virus Virulence and Pathogenicity*, edited by G. E. W. Wolstenholme and C. M. O'Connor. Ciba Foundation Study Group, No. 3, 1960. London.

INTELLIGENCE AND PREMATURITY

It is generally agreed that prematurely born children—those weighing 5½ lb. (2.5 kg.) or less at birth—bear more than their share of gross mental and physical defects, though not all of these are the sequelae of prematurity as such. There is less good agreement about the subsequent mental development of premature children that are not grossly handicapped, the great majority of whom go to ordinary schools.

In an article at page 1008 of the journal this week Dr. J. W. B. Douglas reports that premature children at school make low scores in tests of mental ability and school achievement and gain only half the number of grammar-school places expected of them. But he attributes these considerable handicaps to the complex social aetiology of prematurity rather than to the effects of low birthweight or short gestation. Even the smallest premature children are no more retarded than would be expected when allowances are made for the defects of their home background. A rather similar picture is given by P. A. Harper and colleagues[1] from Johns Hopkins University, who have studied the "intellectual status" of 460 premature children under the age of 5 years. Most of the children were within the normal range of intelligence and it was only among the smallest (weighing at birth 1,500 g. or less), that any appreciable handicap was found. Yet, even among these, 65% were regarded as of average or above average intelligence. A very different picture is given by C. M. Drillien[2] from Edinburgh. She reports a relatively high proportion of dull, retarded, and grossly defective children among those weighing less than 4½ lb. (2 kg.) at birth; below 3 lb. (1.4 kg.) birthweight only 13% were of average or above average intelligence. Few studies of very small premature babies are available, and we do not know whether Drillien's findings are generally applicable or whether they are peculiar to Edinburgh. Since some 15,000 babies of birthweight 4½ lb. (2 kg.) or less and 5,600 of 3¼ lb. (1.5 kg.) or less are born each year in England and Wales, it should not be difficult to get an answer to this question.

The studies by Douglas and by Harper and colleagues were based on a comparison of premature children with mature "controls" matched for factors such as sex, birth rank, and home background. The very word "control" suggests a scientific precision which is illusory. Even the most careful matching of controls can take account of no more than a small part of the broad spectrum of social and biological factors that are associated with prematurity, and, as Douglas has shown, a blind reliance on this method may lead to a false interpretation of results. Control comparisons are a commonplace in socio-medical research and it is important that their limitations should be clearly realized.

If matched controls are unsatisfactory, what alternatives are there? Some have suggested that brothers or sisters make the best controls, but differences of age and birth rank make comparisons difficult.[3,4] Moreover, parents do not treat all their children alike and the amount of social and geographical movement among families is high, so that within the same family different children may have very different opportunities and be subject to very different environmental influences. The most satisfactory solution might well be to compare the selected group (in this case, premature children) with the whole population from which they are drawn, or, if this is impossible, with a sufficiently large random sample of it.

[1] Harper, P. A., Fischer, L. K., and Rider, R. V., *J. Pediat.*, 1959, **55**, 679.
[2] Drillien, C. M., *J. Obstet. Gynaec. Brit. Emp.*, 1959, **66**, 721.
[3] Clarke, C. A., in Symposium on *Natural Selection in Human Populations*, edited by D. F. Roberts and G. A. Harrison, 1959, p. 20, London.
[4] Hess, J. H., Mohr, G. J., and Earlcime, P. F., *The Physical and Mental Growth of Prematurely Born Children*, 1934, Chicago University Press.

DIHYDROSTREPTOMYCIN DEAFNESS

Two years ago T. Cawthorne and D. Ranger[1] reported in this journal 22 cases of disabling vestibular damage produced by streptomycin, sometimes given in doses of only a few grammes, and for doubtful indications, including prophylaxis in connexion with clean operations. In some of these patients the diagnosis implied impairment of renal function, and it is well known that if the excretion of streptomycin is retarded the high resulting blood levels can quickly damage the eighth nerve.

Whereas streptomycin usually affects the vestibular branch of the eighth nerve, dihydrostreptomycin attacks the auditory, with the added difference that the effect is often not produced during treatment, but only develops afterwards at an interval which may be as long as six months. This insidious and even greater danger demands that dihydrostreptomycin be regarded as a drug to be used only for serious indications, if indeed it should not be replaced by streptomycin altogether. That this is far from being an accepted principle, at least in the United States, must be concluded from a report sponsored by the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology,[2] which issues a grave warning against the prescription of this antibiotic, particularly for inadequate reasons and in a disguised form. It is explained that the supposed lesser toxicity of a mixture of streptomycin and dihydrostreptomycin has led to the inclusion of both in proprietary mixtures, usually with penicillin, under non-descriptive names ("combiotic," "dicrysticin," "districillin," "strocillin," "durycin"). The report tabulates particulars of 32 cases in which loss of hearing, usually severe, resulted from the administration of dihydrostreptomycin, either as such or in one of these mixed proprietary forms. A few of the patients had been treated for tuberculosis and the total dose was large, but in the remainder the indication was by no means so clear, and the total dose was small—in 15 patients not exceeding 6 g. The diagnoses given include "influenza," "cold," "bronchial asthma," "furuncles," "sinusitis," "encephalitis," and "mono-

[1] Cawthorne, T., and Ranger, D., *Brit. med. J.*, 1957, **1**, 1444.
[2] Shambaugh, G. E., *et al.*, *J. Amer. med. Ass.*, 1959, **170**, 1657.
[3] Seventh Annual Symposium on Antibiotics, *Lancet*, 1959, **2**, 907.

nucleosis." Undisclosed reasons may account for these oddities in prescribing, but the objective is clear in six cases treated post-operatively, three after hysterectomy and three after appendicectomy. The latter operation may in some circumstances call for antibiotic cover, but for hysterectomy the necessity is at least doubtful, and surely no gynaecologist would adopt this precaution if he knew that it involved any danger of producing permanent disability. Two of these cases are described in more detail: a woman aged 45 was given "combiotic" for four days after an "uneventful" hysterectomy, and one aged 39, who was a telephone operator and naturally "became considerably disabled and depressed over her loss in hearing," had been given "strocillin" twice a day for eight days. Unfortunately nothing is said about renal function in any of these patients; only one diagnosis ("nephritis") suggests impairment, and 20 of them were under 50 years of age.

It is deplorable that such injury can be inflicted on a patient both unnecessarily and inadvertently. This report concludes that dihydrostreptomycin "should be omitted from commercial combinations of antibiotics, or if included its presence should be clearly indicated in the name," and it has recently been reported that official action on these lines has been taken in the United States.[3] No one is likely to dispute this conclusion, but some might be inclined to go further than this, and question whether combinations including penicillin and either dihydrostreptomycin or streptomycin should be marketed. They tend to be used for purposes, especially prophylactic, in which the necessity for them is doubtful, and they have undoubted dangers and drawbacks. Probably much less dihydrostreptomycin is given in this way in Great Britain than has been in the United States, but a patient with deafness of rapid onset might pertinently be questioned about operations or injections within the preceding six months.

EFFECTS OF LENTICULAR IMPLANTS

When the opaque cataractous lens is removed from an eye, clear vision can be restored only if it is replaced by a lens of equivalent convexity, either in front of the eye as the traditional spectacle lens or within the eyeball as an acrylic lenticular implant. The main drawback of the spectacle lens, apart from its clumsiness, is that it magnifies the retinal image, so that it cannot be fused with a normal-sized image from the fellow-eye. In the great majority of cases this is of small moment, since there is little occasion to remove a cataract when the fellow eye is healthy and likely to remain itself free of cataract. But we meet cases occasionally of monocular cataracts that merit extraction, and among them are a few patients whose intelligence or occupation could justify such an implant in the interests of full binocular vision in spite of a further serious surgical hazard.

The idea of replacing the lens of the eye by an artificial lenticulus is not as new as it seems, for in 1766, when Daviel's revolutionary method of extracting the lens had barely taken root, and lenses were still just being dislocated by "couching" them in the old prehistoric way, Casanova recounted how he met a certain charlatan in Warsaw called Tadini who brandished a box of little polished crystalline balls, which he used to insert behind the cornea when the cataract had been dispatched. Poor Tadini was discountenanced by the orthodox, and finished up as a Spanish soldier in Barcelona. Then in 1950 H. Ridley fashioned an acrylic lenticulus which he was able to insert safely and securely behind the pupil, after an extra-capsular cataract extraction, and so restore full binocular vision. After ten years of world-wide trial, the Ridley lenticulus is still being used in carefully selected cases (nearly always monocular cataract in the young adult), but it has too often provoked an indolent and damaging uveitis to find acceptance as a routine procedure. In an attempt to overcome some of its disadvantages, Strampelli, in 1953, fashioned a lenticular implant that could lie in front of the pupil, supported by "arms" which stretch into the angle between the iris root and cornea; and this anterior-chamber implant is now generally preferred to the earlier Ridley lenticulus that lay behind the iris.

How great is the danger of damaging such an aphakic eye by inserting an acrylic lenticulus into the anterior chamber? The final answer must wait many years, but the first pathological study of such an eye has recently been published[2]; and it should curb the exuberance of some of the more determined lenticulus-implanters. This patient was an old man of 71 with a normal fellow-eye, who died from an unrelated cause six weeks after the operation had been performed. The pathological findings by Professor Ashton were impressive: (*a*) The arms of the implant had pushed the iris root so far back, and caused so much atrophy of the adjacent tissues, that a complete tear of the iris root or of its attachment to the sclera (so permitting the implant to slip back beneath the choroid and sclera) would have seemed a possible outcome. (*b*) A large portion of Descemet's membrane had been stripped off at the time of the insertion of the implant, and was found buried in the tissues at the angle of the anterior chamber (this would doubtless have caused no permanent damage, but attests to the considerable trauma of the operation). (*c*) There was strikingly little inflammatory reaction (in contrast to the marked inflammatory response in those eyes that had reached microscopy after a Ridley lenticulus). (*d*) The macula showed gross oedema, attributable to the hypotony occasioned by a second operation so soon after the first.

These findings call for caution, but not, of course, abrupt abandonment of this operation. Perhaps a lenticulus with narrower arms will cause less atrophy of the iris (though such an arm would be sharper and might even cut deeper into the soft uveal bed). Perhaps, in the light of these findings, a modified technique of insertion of the lenticulus would help, or a greater interval between the extraction and insertion. But evidently we should restrict this operation to those few

[1] Ridley, H., *Brit. J. Ophthal.*, 1952, **36**, 113.
[2] Ashton, N., and Choyce, D. P., ibid., 1959, **43**, 577.

cases where the advantages positively outweigh the risks, and we should avoid subjecting too many healthy aphakic eyes to dangers which we cannot truly apprehend until several more years have passed. And we should never forget that distant warning. "Life is short . . . experience fallacious, and judgment difficult."

FELLOWS OF THE ROYAL SOCIETY

Among the 25 new Fellows of the Royal Society elected last week are four medical men and several scientists whose work has advanced medicine.

Professor J. N. Davidson, who has been Gardiner professor of biochemistry at Glasgow since 1947, is a leading research worker on the chemistry of nucleic acids. In a remarkable series of experiments he and his colleagues have lately thrown light on the synthesis, in isolated living cells, of deoxyribonucleic acid, the substance which transmits hereditary information in the nucleus of cells. Sir Stewart Duke-Elder, one of the relatively few surgeons who have ever been elected F.R.S., is director of research at the London University Institute of Ophthalmology. He has for long enjoyed an international reputation as a master of his craft, a fount of lively ideas, and author of a unique classic, the *Textbook of Ophthalmology* in seven volumes. Notable among his researches are those into the intraocular circulation and the related problem of glaucoma. Dr. P. A. Gorer, who is reader in experimental pathology at Guy's Hospital Medical School, has been elected for his work on immunology in relation to tissue transplantation. His elegant researches have thrown light on the antibody reactions to transplanted malignant cells, and how these reactions are related to the genetic constitution of donor and recipient animal. Sir George Pickering, elected for his work in particular on the causes of hypertension, has shown, with his colleagues, that blood pressure appears to be inherited as a graded character in any given population, not as a character with distinct divisions into "normal" and "high." Besides a busy life in clinical and epidemiological research, Sir George has found time to give much assistance as lecturer at home and abroad and in serving on the University Grants Committee. Formerly director of the medical unit at St. Mary's Hospital, he is now regius professor of medicine at Oxford.

Among the non-medical men elected are the following, with the citation that accompanied their election:

Dr. D. G. Evans, director of the Medical Research Council Biological Standards Control Laboratory, London: distinguished for his investigations on the pathogenesis and prophylaxis of anaerobic wound infection and whooping-cough, and for his work on biological standards. Dr. H. E. Huxley, member of external staff of the Medical Research Council, Department of Biophysics, University of London, University College: distinguished for his work on the fine structure of muscle and on the mechanism of muscular contraction. Dr. J. C. Kendrew, deputy director of the Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge: distinguished for his work on the three-dimensional analysis of myoglobin by direct *x*-ray diffraction methods. Dr. E. N. Willmer, reader in histology at the University of Cambridge, Department of Physiology: distinguished for his work on cells, their growth and metamorphosis, and on colour vision.

WELLCOME BENEFACTIONS

More than £800,000 has been distributed in grants by the trustees of the Wellcome Trust during the past 18 months. About half of this munificent sum was allocated by the trustees, whose chairman is Sir Henry Dale, O.M., during the six months from September 1, 1959, to February 29, 1960. The size of the major grants during this period shows the importance the trustees attach to the encouragement of promising research not only in Great Britain but in other countries as well. The largest grant, of £120,000, goes to King's College, London (Professor J. T. Randall, F.R.S.), and will help to meet the cost of establishing a department of biophysics. Professor Randall and his colleagues have achieved outstanding results, despite very restricted accommodation, in their studies of the detailed anatomy of living cells and tissues and of the structure and function of nucleic acids. With the additional space provided by the new premises, King's College will be able to have its own department of biophysics, and the Medical Research Council's unit will also be housed under the same roof.

The University of Toronto (Professor C. H. Best, F.R.S.) receives £70,000 to build and equip additional research accommodation in the Charles H. Best Institute; University College, London (Professor B. P. Medawar, F.R.S.), £30,000 for a research unit in cellular immunity; the Johns Hopkins Hospital, Baltimore (Professor A. McGehee Harvey), £15,000 for a research laboratory in which *x*-ray cinematography will be used in studies of the heart and blood vessels in man; and University College of the West Indies, Jamaica (Professor John Waterlow), receives up to £8,000 for a mass spectrometer for use in the Medical Research Council's tropical medicine metabolism research unit. Research on the physiology of prenatal growth is aided by a substantial grant to Professor A. St. G. Huggett, F.R.S., of St. Mary's Hospital medical school, and departments of virology at Glasgow, zoology and comparative anatomy at Oxford, anatomy at St. Andrews, and physiology at Oxford, will benefit from the expenditure of £34,000 on four electron microscopes.

With these and other benefactions (such as the Wellcome research travel grants) the Wellcome Trust is playing an outstanding part in the support of scientific research of the highest quality and thus is admirably fulfilling the wishes of its founder, Sir Henry Wellcome.

Dr. Gregorio Marañon, professor of endocrinology in the University of Madrid, died on March 28, aged 72. Well known both as an endocrinologist and historian, Dr. Marañon had been a Foreign Corresponding Member of the B.M.A. since 1936.

Drug Treatment of Disease

LOCAL ANALGESIC DRUGS

BY

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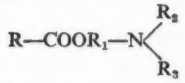
The properties demanded of an ideal local analgesic drug are many and varied. They include rapid onset and adequate duration of analgesia; low systemic toxicity, so that an adequate volume may be injected without exceeding the maximum safe dose; lack of irritation to surrounding structures and without damage to nervous tissues; and effectiveness by all routes of administration. In addition, certain physical properties, such as solubility in water and stability of solution during storage and sterilization are required.

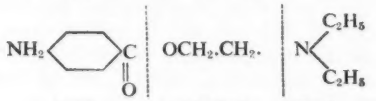
To a great extent this formidable list is satisfied by most modern local analgesic drugs, though some compromise must be accepted. In efforts to attain the ideal a large series of drugs have been introduced, of which a comparatively small proportion have stood the test of time. However, the large number of names of these drugs, and the variety of proprietary names for the same chemical substance, have led to a highly confusing nomenclature. Indeed, it is often difficult to be sure which particular drug is referred to, especially when reading papers from overseas.

Chemistry

The majority of local analgesic drugs are tertiary amino-esters of an aromatic acid, and can be represented by the basic formula:

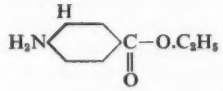


where R represents the acid radical, most commonly *p*-aminobenzoic acid, and R_1, R_2, and R_3 substitution points in the alcohol and amino groups. The best known member of this typical structure is procaine:

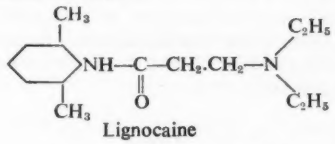


Acid Alcohol Tertiary amine

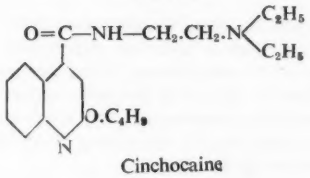
Changes in any part of the molecule will alter the properties of the substance. As a rule, lengthening of the alcohol chain (R_1) or substitution in the amino group (R_2, R_3) produces a more powerful analgesic, but with an increase in toxicity. The presence of the tertiary amine is not essential for producing anaesthesia, and benzocaine is an example of a simple alkyl ester of *p*-aminobenzoic acid:



Not all local analgesics follow this general pattern, and some of the better-known agents such as lignocaine, which is an anilide derivative, and cinchocaine, which is a quinoline derivative, must be placed in a chemical "miscellaneous" group.



Lignocaine



Cinchocaine

Mode of Action

There is general agreement that a local analgesic drug can enter a nerve fibre or cell only in the form of free base. Since the drug is available as a water-soluble salt, usually the hydrochloride, of a basic substance, it has an acid reaction. Hydrolysis must therefore take place before the lipoid-soluble base can be liberated. This is brought about by the alkaline tissue fluids and has led to suggestions that previously alkalinized solutions offered advantages, especially in greater speed of action. Unfortunately such preparations deteriorate rapidly, and, unless alkalinization is carried out most carefully, precipitation of base occurs with resulting loss of activity. Experimentally it has been shown that ionization takes place within the nerve cell, and it is the cationic form of the base which is important. In such a reaction the base changes from a tertiary amino to a quaternary ammonium compound, and many quaternary ammonium compounds have the property of blocking synaptic transmission.

A more precise interpretation of the method by which local analgesic drugs act is not possible, but certain additional facts are known. Impulses in the smaller nerve fibres are blocked before those in larger fibres, perhaps owing to the relatively greater surface area exposed to the drug. Thus in a mixed nerve autonomic and sensory fibres are anaesthetized before motor. A pattern, too, may be seen in the order in which sensory modalities are lost, but great individual variations are encountered.

Toxicity

A local analgesic drug causes toxic symptoms when the rate of administration or absorption exceeds that of elimination. These drugs are destroyed by plasma esterases and by the liver. When a patient has serious liver damage the risk of an overdose is increased. The dose which may be safely administered thus depends not only on the physical condition and age of the patient but also on the site of injection and the particular drug which has been used.

Two types of toxic reactions may be seen, affecting either the central nervous or the cardiovascular system. The most apparent is cortical stimulation characterized by convulsions, which, though impressive, are not as serious as the less obvious effects. Medullary depression may follow, as with an overdose of narcotic drugs. At the same time the myocardium is depressed and a bradycardia proclaims interference with the conduction mechanism. Convulsions, as in other circumstances, can be controlled by intravenous injection of a rapidly acting barbiturate. But this will aggravate existing cardiovascular or respiratory depression. Only a minimal dose of barbiturate should be given, and at the same time it may be necessary to give artificial respiration and restore the blood-pressure. Reactions due to a so-called sensitivity to the drug are probably so rare that they can be ignored.

Drugs

Cocaine, procaine, amethocaine, and cinchocaine are so well known that a detailed description of their properties would be superfluous; these are summarized in the Table below. Some of the more recent additions, however, should be mentioned, for they indicate the way in which chemists are attempting to satisfy clinical ideals in local analgesic drugs.

Lignocaine.—This is an anilide derivative synthesized in 1943. It is reputed to be slightly more toxic than procaine, but, being more powerful, has a higher therapeutic index. It has the advantages of stability in solution and will withstand long periods of storage and autoclaving. To these may be added a short latent period, a tendency to spread, and a *p*H 6.4, which approximates to that of the tissues. It is the only local analgesic drug which causes neither vasodilatation nor vasoconstriction. It is effective in all situations, and without the addition of adrenaline it may be expected to give analgesia lasting for about one and a half hours. The maximum safe dose is about 500 mg., though this can probably be exceeded in healthy young subjects. It is available not only in solution but as a jelly, ointment, and a viscous solution for topical application.

Carbocaine.—Synthesized in 1957, and, like lignocaine, is of Swedish origin. The drug is very similar to lignocaine in both its properties and chemical formula, but is said to be effective for rather more than two hours when used without a vasoconstrictor. It is also reputed to be free of undesirable systemic side-effects.

2-Chloroprocaine.—First described in 1952, 2-chloroprocaine attracted interest for the very rapid onset of analgesia it produced and its high therapeutic index. Low toxicity is due to the rapid destruction which takes place in contact with plasma. This necessarily limits the duration of effect, which without the addition of adrenaline may not exceed 20–25 minutes. It is a reasonably stable compound with a *p*H of 4.9.

Hexylcaine.—This drug was synthesized in 1944 and has enjoyed a considerable vogue as an agent for surface analgesia. It is moderately stable and withstands autoclaving. Toxicity is low and the duration of analgesia about two hours. Unfortunately, solutions have a low *p*H, and this acidity accounts for soreness and tissue irritation sufficient to limit use by injection.

Ravocaine.—This is a procaine derivative which is considered to be a better topical agent than cocaine and to have a toxicity similar to that of amethocaine (i.e., maximum safe dose about 150 mg.). It has been used in a concentration of 0.1% for infiltration and 0.5% for nerve blocks, particularly in dentistry.

Piperocaine.—This achieved a certain fame when used as a 1.5% solution for caudal and extradural injections by virtue of the rapidity with which analgesia developed in these situations. Having a toxicity only slightly greater than that of procaine, and a duration of effect of about 45 minutes, its use led to a revival of interest in these methods of analgesia.

With the exception of lignocaine and piperocaine, these newer drugs are not freely available in the United Kingdom, but the following Table summarizes information on those which are in common use in this country.

Drug and Synonyms	Uses	Maximum Dose	Duration without Adrenaline	Concentration or Dose
Cocaine ..	Topical only	200 mg.	20 min.	4–10%
Procaine: Ethocaine .. " Novocain " " Planocaine " " Neocaine " " Sevicaine " " Novutox "	Infiltration*. Nerve blocks*. Occasionally spinal analgesia	1 g.	20 ,,	>0·5–2% 100–200 mg.
Amethocaine: Pantocaine Pontocaine Tetracaine " Anethaine " " Decicain "	Nerve blocks*. Infiltration*. Spinal. Topical	150 mg.	2 hr.	>1/1,000–1/2,000 5–15 mg. 2%
Cinchocaine: " Dibucaine " " Nupercaine " (" Percaine ")	Spinal. Nerve blocks*. Infiltration*. Topical	150 ,,	2½–3 hr.	<1/1,500 (light) 1/200 (heavy) 1/1,000
Lignocaine: Lidocaine " Xylocaine " " Xylotox "	Extradural and caudal. Nerve blocks. Infiltration. Topical. Spinal	500 ,,	1½–2 hr.	>1·5% >0·5–2% 4% 2–5%
Piperocaine: " Metycaine "	Extradural and caudal	1 g.	45 min.	>1·5%

* Addition of a vasoconstrictor advisable.

Local Analgesics for Prolonged Effect

Unhappily, though the demand for such agents is great, few are available which will produce long-acting analgesia without undesirable side-effects. "Depot" solutions in wax bases, mucates, and ammonium compounds have all been tried without much success. Hopes were raised by the introduction of efocaine, which was a combination of procaine base and procaine hydrochloride in a solvent. In spite of many apparent successes this drug was held responsible for a number of disastrous neurological sequelae, and on these grounds it, too, had to be abandoned. Oily solutions containing both a water-soluble salt of a local analgesic and benzyl alcohol, which causes some degree of nerve destruction, are still used, but their duration of action is somewhat variable and uncertain.

Alternatively, one must turn to alcohol and phenol, neither of which are strictly analgesic drugs. They cause analgesia of long duration only by virtue of nerve destruction. The intrathecal injection of alcohol to relieve the intractable pain of carcinoma has proved quite successful. Some disturbance of sphincters may follow but it is temporary in most instances. When injected into peripheral nerves, an efficient block may be produced, though it is sometimes followed by an unpleasant alcoholic neuritis which may persist for five to six weeks. 6% phenol solutions have been tried as an alternative, and, though the results are not so certain, they are accompanied by less disturbance and pain.

Such solutions are most effective in smaller nerve fibres and can produce a chemical sympathectomy lasting up to a year when injected into the lumbar sympathetic chain.

Vasoconstricting Drugs

No description of local analgesic drugs can be complete without mention of the vasoconstrictors which are commonly added. The function of these drugs is twofold: to prolong the action of the analgesic drug, thus reducing the rate of absorption, and hence, at the same time, reducing the risk of toxic reactions. In fact, it is a safe rule to add a vasoconstricting agent when injecting any local analgesic which causes vasodilatation.

Adrenaline is still the commonest drug used in spite of not infrequent systemic side-effects. These reactions are usually the result of overdosage or inadvertent intravenous injection. Adrenaline is most frequently marketed in a 1/1,000 solution, and strict observance of 0.5 ml. as the maximum dose (0.5 mg.) will much reduce their incidence. For most purposes a concentration of 1:200,000 is adequate, and even 1:600,000 can produce efficient vasoconstriction if given sufficient time to act. Adrenaline is difficult to sterilize and readily decomposes. Thus its addition to a local analgesic solution, unless this is freshly prepared, requires an acid *p*H, which in turn leads to irritation of tissues and pain on injection. However, the alternatives such as phenylephrine, which is reputed to have little effect on the heart or cerebral cortex, and cobefrin, which produces less vasoconstriction and cannot be autoclaved, have found little favour in Great Britain.

Mucolytic Enzyme

Hyaluronidase is the mucolytic enzyme which breaks down hyaluronic acid and provides a greater area of distribution for injected drugs. When used with local analgesic solutions it provides a more extensive field of analgesia and rapid penetration of nerve fibres. But, since absorption may take place from a larger area, the duration of analgesia is shortened and the toxicity increased. While having obvious possibilities, this drug should never be used as an excuse for a poor technique and an inadequate knowledge of anatomy.

Choice of Drugs

Procaine may still be used most commonly, but lignocaine, in spite of a relatively higher cost, is more efficient and convenient for general use, quite apart from being the undoubted drug of choice for extradural analgesia.

If vasoconstriction and shrinkage of mucous membranes is required for ear, nose, and throat surgery, cocaine retains pride of place for topical application. But if vasoconstriction is unimportant, lignocaine, amethocaine, and cinchocaine all have their adherents, who base their preference on a fear of the toxic reactions from cocaine.

For spinal analgesia cinchocaine or amethocaine offers a duration of effect adequate for most surgical procedures. Lignocaine would not appear to have any particular advantages in this method of analgesia except in the conduct of a continuous spinal block maintained with serial injections. Whatever the merits or otherwise of spinal analgesia, there is little evidence that any particular drug in use to-day can be blamed for the post-spinal sequelae which have tended to bring the method into disrepute.

The limitations of the various drugs available having been accepted, the choice will probably be determined by such practical considerations as expense, convenience, and familiarity. Each drug has its own particular advantages, but an understanding of their properties and limitations will lead to more efficient analgesia and fewer undesirable side-effects.

RESIDENTIAL CARE OF MENTALLY HANDICAPPED CHILDREN*

BY

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There are 60,000 mental defectives in institutional care in England and Wales, of whom 8,500 are children, mainly of idiot or imbecile grade. It is widely thought that because of the increased emphasis upon home care for the mentally subnormal the numbers going into institutions are likely to fall in the near future. While this may be true of adults, who for the most part present rather different problems, I do not think it is true of children. The number of severely subnormal children who survive infancy has almost certainly increased markedly in recent years: four times as many mongols, for example, survive until the age of 10 years to-day as did in 1929 (Carter, 1958). Moreover, even to-day the number of mentally subnormal children who go into mental deficiency hospitals is arbitrarily restricted by the number of beds available. The pressure to find more places is bound to grow—and is likely to prove irresistible. It is therefore a matter of public concern how we can best look after these children, and how far their potentialities can be realized.

Both in this country, which probably leads the world in this field, and in other countries, which have mostly modelled their practice upon ours, mental defectives in residential care are usually housed in large comprehensive institutions or "colonies" containing up to 2,000 beds. Some hospitals have only children and others only adults; but most contain children and adults, and both high-grade and low-grade cases. The pattern of institutional care has not changed very much over the last century. Though there is to-day much discussion about hostels, large institutions are still being built, and existing large institutions are being increased still further in size. Few attempts have been made during the past 30 years to think out the basis of our policy of institutional care and to see what changes are desirable to bring it into line with changing mental health needs and our increased understanding of these.

Present Study

In August, 1957, I had the opportunity—through the generosity of the National Society for Mentally Handicapped Children, which provided a grant for a three-year research project—to begin a study of psychological and educational problems of imbecile children. The study of residential care which is described here forms part of this research, and has been carried out in a 16-bed unit under the control of the

*Based on a paper read to the British Association for the Advancement of Science on September 7, 1959.

Fountain Hospital, London. The Fountain Hospital has made available the building in Reigate and the staff, and has been responsible for general administration and for running-costs. Miss Patricia Daly, a nursery-school teacher in the research group, has been the driving force in putting the scheme into action; and Dr. J. G. Lyle, a research psychologist, has made psychological assessments of the children, and has carried out a survey of imbecile children in institutions and at home.

The children in the unit were between 4 and 10 years of age on entry, but mentally they were between about 18 months and four years. We have treated them according to their mental rather than their chronological age, and we have tried to model our practice upon patterns evolved by the Children's Department of the Home Office (1955) for the residential care of young normal children of comparable mental age.

Why did we choose to treat our imbecile children aged between 4 and 10 years chronologically as though they were normal children aged between 18 months and 4 years?

Half a century ago the great French psychologist Alfred Binet showed that mental defectives resembled, in intelligence at least, ordinary children of a much younger age. Though no scales comparable to intelligence tests exist for the measurement of non-cognitive psychological qualities, observation of imbecile children strongly suggests that emotionally and socially they are also very backward, and that here, too, they are like much younger normal children. It can be argued, therefore, that the methods of education and care suitable for young normal children should also be appropriate for older imbecile children. In so far as this is so, it is to the nursery school that we should turn for ideas of how to teach mentally handicapped children, and upon the residential nursery that we should base our methods of residential care.

Day "Occupation" Centres

In general the pattern of education found in day "occupation" centres bears little resemblance to that which has evolved, after half a century of intensive activity in Europe and the United States, to meet the needs of normal pre-school children. The occupation centre is modelled on the infant school or even junior school, rather than on the nursery school, though the content of the lessons is of course simplified to meet the supposed intellectual needs of the mentally handicapped. The day is arbitrarily divided into the short periods; formal lessons are given in speech-training, handwork, physical education, and sense-training; and in many occupation centres little time is allocated to play, except in the youngest groups. The approach is excessively didactic and formal, and the searching criticisms which have been made by those with experience with young normal children of the whole conception of education that favours such methods have been largely ignored by those responsible for the curriculum of most occupation centres.

Whether the effect of our present method of training in the day occupation centre is to retard the emotional, social, and physical development of mentally handicapped children one cannot say, because practically no research into alternative methods has been carried out. What we do know, however, is that our methods of *institutional* care have a crippling effect upon them. Dr. Lyle has shown that institutional children are particularly retarded in all aspects of language and speech, and in verbal intelligence, as compared with similar mentally handicapped children who live at home. The older the children the greater becomes the discrepancy between their achievements and abilities and those of comparable children brought up in their own homes. The same is true of their personal independence—that is, of their ability to dress themselves, manage their own meals and toilet, and generally help both themselves and the adults who are responsible for them. Observation shows them also to be extremely backward socially and emotionally; and it is clear that in these and in other ways institutional care to-day warps and stunts the development of already seriously handicapped children.

At the end of the war the Curtis Committee investigated the pattern of care offered to normal children living in institutions and homes other than their own. They, too, found backwardness and neglect, brought about, as with our mentally handicapped children to-day, not by ill-treatment or lack of concern on the part of those who cared for the children, but by staff shortages, large units, and general ignorance of principles of child upbringing. After the Report of the Curtis Committee (1946), and the Children Act of 1948, the basis of our policy of care for normal children has changed; and to-day it is recommended that those (ordinary) children who cannot be fostered should be brought up in "family group homes" (which may take children of all ages) or in residential nurseries (for the under 5's).

It seemed to us, first, that imbecile children in general might properly be given the same kind of educational diet as normal pre-school children; secondly, that so far as residential care is concerned the criticisms of the Curtis Committee (which excluded the mentally handicapped from its terms of reference) could apply with at least equal force to the mentally subnormal; and, thirdly, that the new pattern of care evolved by the Children's Department of the Home Office was an appropriate model upon which to base a system of residential care for those mentally subnormal children who require it.

Family-care Pattern

The residential nursery in particular, designed to provide as satisfactory a substitute home-life as possible for groups of ordinary children under 5 who could not be individually boarded out, appeared likely to meet the needs of mentally handicapped children and to avoid the major disadvantages inherent in our present methods of hospital care. In such a nursery the numbers can and must be small—not more than 30 children and if possible not more than 20. The children are divided into small groups or "families," and so are not constantly subjected to the excitement, clamour, and impersonal regimentation which comes with large numbers. They are cared for by housemothers, whose training and experience are in the management of problems of normal children, rather than by nurses; and because of the small numbers of children in a group the housemothers are able to give individual children the affection and care they need to satisfy their physical, emotional, and intellectual needs. It is believed that, by

living in a "family," the children learn more easily the skills necessary for social life in a wider community. The pattern of family care in which one or two adults have the full responsibility for a small group of not more than four to eight children has been shown to have a beneficial effect upon the development of young normal children, and it seemed almost certain that mentally handicapped children would benefit at least as much from this type of care.

There were other reasons why the residential nursery pattern appealed to us. A small unit can be sited in a town or city, near the child's own home. It is therefore easy for parents to visit and to take their children home for the day or for holidays. Thus the children remain part of their families and of the community. Again, it is becoming increasingly difficult to find staff for mental deficiency institutions in the country miles from where the bulk of our highly urbanized population choose to live; but to build new hospitals in cities would be impossibly expensive even if it were desirable. We think it would be easier to attract suitable staff to small units in urban areas; and, because a small unit is less inherently bureaucratic than a large one and the staff can be given more responsibility and independence, good people are more likely to stay.

For these reasons, therefore, in setting up an experimental unit for mentally handicapped children we decided to follow, and to adapt where necessary, the staffing ratios and the methods of child care that are employed in residential nurseries for pre-school children of normal intelligence.

Procedure

As a first step 32 children, divided into 16 pairs matched for sex and age, I.Q., and so far as possible type of defect, were selected to take part in the study. Children with severe physical problems and those suffering from psychosis were excluded, since in a pilot study with largely untrained staff it was not felt possible to include children who presented special nursing or management problems. With these important exceptions those selected were a representative sample of imbecile children in the Fountain Hospital. One child from each of the 16 pairs was chosen by lot to go to the new unit, so that each "experimental" child has a matched control who has remained in the Fountain Hospital.

There are nine boys in the group and seven girls. Half of them are mongols, one is a phenylketonuric, and the rest suffer from undiagnosed conditions all thought to involve severe brain injury. Their average age on entry to the unit was 7½ years and their average I.Q. was less than 25 points on the verbal scale of the Minnesota Preschool Intelligence Test, though on the non-verbal scale the mean was about 40 points. In personal independence, measured on a standardized age scale, they averaged about 3½ years. All were in good or fair health.

The unit to which the experimental group were sent is a large detached house in Reigate. It has lovely grounds, but the house is in many ways not ideal—for example, there is only one small staff room for use both as a dining-room and as a sitting-room; and it is of course far from the parents' homes, which makes visiting difficult. The staff at first consisted of a nursing sister trained in mental deficiency (who, however, had had little experience with children, either normal or subnormal) and a varying number of nursing assistants, also lacking experience with children. We had no opportunity of discussing the programme with the staff before the first eight children arrived, and there was practically no equipment, except some orange-boxes, for the children to play with.

During the early weeks we were, as we have often been since, short of staff, and a series of relief staff were used to help out. This meant, for example, that in the first week there were 13 different adults looking after the children, as well as several visitors and other adults such as domestics and the handyman not directly concerned with the children. So much for continuity of care in the early stages.

The children and the staff were just beginning to adjust to the new conditions when the numbers were increased to the full complement of 16, and this again resulted in a serious setback. For among the later arrivals there were several very unruly and disturbed children whom the staff found great difficulty in controlling. It has taken a full year and more for the children to settle, for us to get the nucleus of a competent and stable staff, and to build up suitable equipment.

The pattern of care even after 18 months is still evolving rapidly, and many difficulties have not yet been finally straightened out. Owing to the staff shortages and lack of suitable staff, it is, for example, only recently that we have been able to introduce the practice of family care, our four capable and keen day staff each being personally responsible, so far as is possible, for four individual children, differing in age and sex. It is only now, therefore, that the change from a hospital-ward type of approach to something resembling a true residential nursery is being effected.

Daily Programme

The first changes to be introduced in the management of the children were in the day's programme. This has been based throughout on nursery-school lines, and there is no formal curriculum. Large portions of the day are spent by the children in supervised play in which they themselves select from the materials and activities available those that interest them. When they tire of one activity they engage in another. In this way, motivated by interest, they learn the motor and social and language skills that will serve them throughout life.

There are, of course, group activities, too, in which the children are encouraged to participate and in which most of them do—though not every child does so every day. In general the day is divided by the routines of toileting and meals, mid-morning drink, the after-dinner rest, story and music, bath-time, and bedtime; but within this ordered division of the day which gives a uniformity and consistency to the children's lives there is a great deal of variety. Outdoor activities such as swings and the sand-pit, water-play and paddling-pool, tricycles, play with a wheelbarrow or boxes, walks and shopping with an adult, and a weekly visit to the zoo or for a picnic in the country by a small group of children—these are the activities that the children particularly like. In them they are exercising their bodies and their minds, learning to talk about their

experiences, and developing the self-control that makes sustained concentration on a particular task possible.

At other times most of the children help about the house, just as normal children do. They will help an adult to make a bed, sort the linen, or set the table, or they will do small errands for their housemother. These tasks have both an educational and a social function. In carrying them out the children learn how a home is run and how to contribute to the general welfare. They have in such situations opportunities for intimate contact with their own particular adult, talking to her and participating with her in some grown-up and therefore important and responsible activity. Even children who are very young mentally get a special pleasure from such activities if they are not burdened with them or made to persevere beyond their span of attention.

There are also opportunities for many creative activities, such as painting, clay, an indoor sand-pit, doll-play, boxes and blocks, story-books, jigsaw puzzles, dressing-up clothes, and other activities and equipment of a kind found in the modern nursery school. In using and sharing equipment the children are learning all the time—and the development of their play has followed the same kind of sequence and shown the same kind of maturation as does that of normal children.

The development of a rich educational programme is still going on. There are many problems—for example, the fact that the children are much bigger and stronger than normal children of the same mental age means that they are in some ways harder to manage. They cannot be picked up and removed physically from a situation as a toddler can, to cite one instance—and the kind of play equipment they need has to be larger and stronger than that designed for the average 3-year-old. Again, their backwardness in speech makes it more difficult for them to share, to request, and to explain. Thus social and emotional development are linked with intellectual development and the use that can be made of the tools of speech.

No attempt will be made here to describe in detail the kind of programme we follow, the difficulties that one must expect to encounter, and the kinds of solutions to some of the problems we are working towards. The major problem, which has troubled us greatly, as it does all who are concerned with residential care, is to find and keep good staff. We are still short of staff; but those we do have are doing a responsible and exacting job in a way that one must admire and respect.

Results

The most striking and pleasing effect of this ordered but free regimen upon the children has been in their social and emotional behaviour. When they first came they were largely mute except for cries and single harsh shouts; they could not play with other children, take turns, or bear frustration. Most would hit out, some would bite, and nearly all flew into violent rages if crossed. Their contacts with adults were superficial and fleeting, and they showed, naturally, no preferences for one adult rather than another. They were unable to concentrate, and would drift aimlessly from one activity to another. They were destructive and aggressive, and tried the patience of the staff to breaking-point.

As the children had been suddenly transported to a completely unfamiliar physical environment, having a very different social climate from any they had been used to, their disorganized and regressive behaviour came as no surprise. What I did find alarming, however, and what in the early days made me wonder whether the venture could succeed at all, was the abnormal, wanton destructiveness of the children and their intense and unpredictable aggression. Not only would they break the equipment, and kick, hit, and bite adults and other children, sometimes with no apparent provocation, but very often a child would fly into uncontrolled storms of anger or grief in which he would beat his head against a wall or bite an arm hard enough to draw blood. The children could not be comforted once an outburst started—and in several children they occurred with distressing frequency and to a degree that I had never seen before. So marked was this behaviour that I wondered whether in some cases it was not an intractable psychotic condition rather than mere mental defect which had brought them into institutions in the first place. One child—the oldest in the group—had in fact to be returned to the parent hospital because in those early days she was such a disruptive influence that she succeeded in occupying the full attention of one member of staff throughout the whole day. (Another epileptic child was also returned on medical grounds at the same time.) But most of the children except the youngest (who had been petted and mothered in his ward in the hospital) displayed to a greater or less degree patterns of grief and anger normally seen only in very young babies; and it was the emotional immaturity of the children rather than their intellectual backwardness which presented the greatest problems.

It has been mentioned that two children had in those early days to be returned to the parent hospital. This we did with reluctance, and their places were taken by two other children for whom controls were found. I believe that both of the children who were returned could have been assimilated in the unit had we not at that time been fully occupied with the administrative problems involved in establishing a new unit, or alternatively if the staff had been more experienced or the children younger. Our evidence suggests that in general it is the older children, with a longer institutional history, who are the most maladjusted. If this is so it might be that many of their difficulties could be prevented if a different pattern of care was adopted. One of the strongest arguments for the family-group method is indeed that it is said to have lessened the incidence of maladjustment in normal children in care.

To-day the old "pathological" behaviour has largely gone; nearly all the children can enjoy simple group play with other children for long periods; they talk quite a lot among themselves; and they are affectionate and happy children, usually busy and interested in what they are doing. They are energetic and full of fun. They are for the most part docile and easy to manage; and they are fond of the staff and the staff of them. If the contrast sounds too good to be true it is because the change itself has exceeded our expectations.

For these changes in social and emotional behaviour we have only qualitative, descriptive records. But for cognitive behaviour some more objective records are available. After one year the children had increased eight months in "mental age" as measured on a verbal intelligence test, as against three months for the controls. In personal independence they had increased six months

as against three months for the controls. No difference was found in increments of non-verbal intelligence, but in all behaviour involving language the experimental group were ahead.

These test results, obtained during April, 1959, are already somewhat out of date, since during the summer the children have shown an accelerating development; and we fully expect that at the end of the second year of the study the contrast between the two groups will be more marked

Implications of the Research?

I shall mention only four points.

First, the study has already shown that it is possible and desirable to bring up imbecile children in small units in which they receive much more individual attention than can be given in a large institution. The administrative implications are far-reaching, and we are at present studying some of them in detail. One point which must be mentioned relates to costs. Daily costs per child are likely to be higher than those of the large institution. They may, however, not be so large as would at first sight appear. For the costs of building and maintaining small homes are likely to be much less than those of large ones. In a large institution there are concealed fixed costs which are often heavy, and even so far as staff are concerned the costs may not be much greater. The Fountain Hospital, for example, has a nurse/patient establishment of 1 : 3. In a small residential home the ratio might be 1 : 2½. If more use was made of the general medical services there might be an overall saving on medical costs. Again, if some units took weekly boarders and others kept school holidays (like residential schools for the educationally subnormal) overall costs might be considerably reduced and the staff problems eased. Finally, if, as a result of closer contact with parents and a more rapid socialization of the children in care, some parents were able to have their children home again after a year or two, there might be an overall saving in the number of institutional places required, and consequently in the cost of residential care.

It is not suggested, on the basis of a single experience with a small unit, that the mental deficiency hospital has no place in a modern health and education service. But we do think that the role of the large hospital should be examined afresh, just as the role of the large orphanage was examined by the Curtis Committee and by Lewis (1954). It is clear, even now, that the mental deficiency hospital is no longer a necessary part of our health and education service as it was in the past. An alternative system in which healthy imbecile children in need of care were given the same facilities and opportunities as ordinary handicapped children deprived of normal home life, with idiots and sick or bedfast children placed in *small* long-stay annexes to children's hospitals, seems perfectly feasible. The merits of such a system are clear enough; and before further hospitals are built one would like to see the alternatives examined, and further empirical studies carried out on a wide scale.

Secondly, we believe that a very different type of educational programme from that generally adopted in occupation centres for mentally handicapped children might meet their needs better, and help them to realize their limited potential more fully. It is not suggested that imbeciles should throughout life be treated as nursery-school children—in adolescence a different programme is obviously called for, to prepare them for work and adult life. We think, however, that those who begin this training too early make a profound educational mistake. They fail to satisfy the children's everyday physical, emotional, and social needs; and they ignore the importance of maturation. There is no evidence that the unending formal lessons in sense-training, toilet-training, social training, speech-training, and the like, to which countless imbeciles have been subjected, have done many of them much good. Common observation and psychological theory alike suggest that normal children do not learn these skills by being taught them in class, and our experiment suggests that imbecile children do not either. We think that it is not until they are adolescent that they are likely to be mature enough for classroom work; and, until they are psychologically "ready" for it, attempts at formal education are not only useless but harmful.

Thirdly, the psychological development of handicapped children is undoubtedly capable of being profoundly modified by changes in their management, and it is possible that some of the most harmful effects of our present methods of institutional care could be mitigated if a more enlightened policy was followed. In the present study we have been particularly impressed by changes in emotional and social development as well as in physical health; but other studies—for example, Clarke and Hermelin (1955)—have drawn attention to the plasticity of even the most severely handicapped persons, sometimes after years of institutional neglect.

Finally, there is a great need for research in this field. Our own studies have, of course, barely touched the problem, and I am afraid that in trying to present some of our findings briefly I may have appeared to overstate the case. By wise management, and with the best of staff, we will not "cure" these children. But we are making it possible for them to live much richer and happier lives—and I have no doubt that this experience, gained during childhood, will enable them when they reach adolescence and adult life to be more useful and productive members of the community than would otherwise have been possible. Some will work in sheltered workshops, one or two perhaps may even be employed in the open market; all are likely to be more mature, more independent, less fearful and neurotic, and more socially competent. I have no doubt that through research we can find ways of easing the problems of the mentally handicapped and their families; and I hope that in doing so we may also find out things about normal children and their development.

Most of the work described here has been initiated and carried out by my colleagues Miss Patricia Daly and Dr. J. G. Lyle, in collaboration with the staff of the Fountain Hospital and the health authorities of Middlesex (where the testing of imbecile children living at home was carried out). The research is financed by the National Society for Mentally Handicapped Children, and the grant is administered by the Mental Health Research Fund. I am grateful to these bodies for their sponsorship of the research and to the Medical Research Council, which has allowed me to participate in it.

I am particularly grateful to Dr. L. T. Hilliard, physician-superintendent of the Fountain Hospital, who first urged me

to consider the psychological and educational problems of imbecile children and who has throughout the present study given us encouragement, criticism, and support, and to Dr. Cyril Williams, of the Fountain Hospital, who has been closely associated with the study at every stage.

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TELEVISION-VIEWING HABITS OF CHILDREN WITH AND WITHOUT DEFECTS OF VISION

BY

L. H. G. MOORE, M.B., Ch.B., D.O.M.S.

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During the past year schoolchildren who attended the central clinic in Dudley for an eye examination were asked how long they had had a television set and how many hours in each week they viewed the programmes. The ages of the children ranged from 7 to 18, and 496 consecutive patients were questioned.

In order to compare these figures with a control group, the help of the teachers of several Dudley schools was sought. The same two questions were put to every child who had been medically examined at school within the previous 12 months, whose recorded vision was 6/6 in each eye, and who had not complained of any discomfort that would have warranted a visit to the eye clinic. The number of children questioned at school was 816.

Table I shows the viewing habits of the two groups of children. The type of refractive error found is shown in Table II, and in Table III the type of refractive error is correlated with the number of viewing hours. The total numbers of hours of television viewing were calculated for each child from the product of the number of hours in a week the child viewed and the length of time the family had had a television set.

The population of the Borough of Dudley is 64,530. The school population is 11,024. The total attendance of schoolchildren at the eye clinic in 1958 was 1,130, and 125 of these attended more than once; therefore the total number attending in the year was 1,005. The maximum period marked on the child's record card before re-examination is one year.

These figures show that there is no basis for the assumption that prolonged television viewing is responsible for an increase in errors of refraction in children. The number of cases of myopia does not appear to increase as the number of viewing hours rises. The figures of errors of refraction closely follow those reported by McNeil (1955) from the school eye clinic at Barnsley in 1953. He found that between the ages of 10 and 15 half the cases reported for the first time were myopes.

The average age of all the children with visual defects in our survey was 11.6 years. The age of the children in the control group must have been very similar, because these 816 children had all had their second school medical examination within the previous 12 months and had been recorded as having no defect of vision. They were therefore all over 10 years of age and under 12.

The B.B.C. television service in the Midlands began in 1949, and has so far broadcast for more than 25,000 hours. The television service in Barnsley began in October, 1951. The pattern of development of errors of refraction does not appear to have been altered by the impact of television.

I am grateful for the co-operation received from Dr. R. M. Ross, the Medical Officer of Health, and his staff, and from Mr. H. W. Eisel, the Director of Education, and his teachers. I thank Dr. R. M. Archer for his help in the clinics, and Mrs. G. Beech, our school nurse.

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TABLE I.—*Viewing Habits of 496 Schoolchildren with a Defect of Vision and of 816 with No Defect*

Total No. of Hours	Children with Visual Defects		Control Group	
	No.	%	No.	%
0– 1,000	187	37·70	214	26·22
1,001– 2,000	101	20·36	122	14·94
2,001– 3,000	85	17·13	170	20·83
3,001– 4,000	35	7·05	98	12·00
4,001– 5,000	35	7·05	84	10·29
5,001– 6,000	18	3·62	53	6·49
6,001– 7,000	14	2·82	34	4·16
7,001– 8,000	8	1·61	17	2·08
8,001– 9,000	5	1·00	10	1·22
9,001–10,000	6	1·20	4	0·49
10,001–11,000	2	0·40	1	0·12
11,001–12,000	0	0·00	6	0·73
Over 12,000	0	0·00	3	0·36

TABLE II.—*Errors of Refraction in 496 Schoolchildren*

Refraction	No. of Eyes	Percentage
Hypermetropia and astigmatism	188	18·95
Hypermetropia	162	16·33
Hypermetropic astigmatism	91	9·17
Emmetropia	69	6·95
Mixed astigmatism	64	6·45
Myopic ,,	30	3·02
Myopia	249	25·10
Myopia and astigmatism	137	13·81
1 Aphakia. 1 Prosthesis	2	0·2

TABLE III.—*Error of Refraction in 990 Eyes in 496 Schoolchildren Correlated with Viewing Habits*

Refraction	No. of Hours of Television Viewing									
	0– 1,000	1,001– 2,000	2,001– 3,000	3,001– 4,000	4,001– 5,000	5,001– 6,000	6,001– 7,000	7,001– 8,000	8,001– 9,000	9,001– 10,000	10,001– 11,000
Hypermetropia and astigmatism	76	38	23	9	18	8	6	3	2	5	0
Hypermetropia	74	26	35	6	8	5	3	1	1	3	0
Hypermetropic astigmatism	35	20	14	8	4	0	5	0	3	0	2
Emmetropia	21	23	9	3	7	2	2	2	0	0	0
Mixed astigmatism	22	15	10	8	6	2	1	0	0	0	0
Myopic ,,	15	9	0	2	0	2	1	1	0	0	0
Myopia	81	50	55	20	15	11	5	3	4	4	1
,, and astigmatism	49	21	24	13	12	6	5	6	0	0	1

SIR CHARLES HASTINGS LECTURE

PROGRESS IN CHEST SURGERY

In Swansea on March 31 Sir CLEMENT PRICE THOMAS gave the Association's Sir Charles Hastings lecture before a large lay and medical audience. He discussed the progress of chest surgery under the title "Yesterday, To-day, and To-morrow." The B.M.A. was more than a medico-political body, said Sir CLEMENT. It was a forum in which the advances in the art and science of medicine were brought before the members and in which these things were freely discussed, so that all within its circle were kept fully abreast of the astonishing progress continuously taking place. It was of this progress he would speak.

Three Swansea Surgeons

Three surgeons with whom he had worked intimately had stemmed from Swansea or its relatively near neighbourhood. The first was Arthur Evans, who was born in Neath. The other two were Morriston Davies and Tudor Edwards. Morriston was the pioneer of chest surgery in Britain, and at 80 remained its doyen. He performed the first planned major operation for pulmonary tuberculosis in this country in 1912, a thoracoplasty on a patient whom Sir Clement had seen 27 years later in good health. Tudor Edwards had been born in Swansea. His devotion to his profession had been single-minded: "his great contribution to his specialty lay in his untiring efforts to disseminate his knowledge by lecture and publication." It was through the many physicians and surgeons in this field whom Tudor Edwards had trained—Sir Clement among them—that his life work was perpetuated. It was for the vision of these early pioneers that we must be deeply grateful.

What a difference there was to-day! In the early thirties the common conditions met with in thoracic surgical wards were empyema, lung abscess, and pulmonary tuberculosis. To-day in most parts of the country the first two were uncommon and the third much less common. Why? In one word, the answer was "drugs." The saga of the control of pulmonary tuberculosis was known to many: in England and Wales in 1947 the mortality was 473 per million living and new notifications were 47,186; in 1957 the figures were 95 per million and 28,870—a reduction of the mortality over 10 years to one-fifth.

Prevention of Lung Cancer

But during these years there had been a great increase in cancer of the lung. What could be done to prevent a disease of which the cause was unknown? Clinical experience suggested that there were factors which tended to initiate malignant conditions in various sites in the body. There was very strong evidence to suggest a close causal relationship between both cigarette-smoking and atmospheric pollution and cancer of the lung. "It seems to me reasonable to accept these evidences at their face value," said Sir Clement. He then proceeded to review some of the spectacular advances in cardiac surgery during the last 10 years or so, mentioning specially Sir Russell Brock's pioneering work in this country and the development of heart–lung machines and hypothermia which had so greatly facilitated operations on the heart. Turning more to the future, Sir Clement mentioned the surgery of coronary artery disease. "We still await a direct attack on the diseased vessels themselves. This will surely come one day," he said.

In conclusion, Sir Clement warned against the scientific problems of medicine blinding doctors to its human aspects. Besides the technical skill which was a prime necessity for success, there were other qualities which went to the making of a good doctor: he must be able to inspire confidence in his patient, understand his fears and hopes; he must also have absolute integrity so that his patient could fully trust his every dictum; and, finally, he must realize that literally the patient put his life in the surgeon's hands when he agreed to treatment. Nothing short of the best would suffice.

Nova et Vetera

AN EARLY RUSSIAN HEART-LUNG MACHINE

In the development of the heart–lung machine for extracorporeal circulation the contributions of the distinguished Russian scientist, Professor S. S. Brukhonenko, have not hitherto received the recognition they deserve. His approach to the problem began fortuitously in 1923 when at the State Institute for Chemistry and Pharmacology in Moscow he was studying the trypanocidal drug suramin ("Bayer 205," "germanin," "nagonal").[1,2] Finding that this drug was capable of producing an "artificial haemophilia," he began to use it as an anticoagulant in blood transfusions.[3] It is noteworthy that at this time he was using roller pumps in his work on transfusion.

In 1926, in collaboration with S. Tchetchuline, he designed an apparatus for the "artificial circulation with blood of warm-blooded animals."[4] The apparatus consisted of two mechanically operated diaphragm pumps with a system of valves. The excised lungs of a donor animal, rhythmically inflated, acted as an oxygenator. One pump delivered venous blood to the oxygenator, the other pumped blood therefrom into the systemic circulation of the perfused animal. The blood of the donor and the experimental animals was treated with suramin.

In the succeeding years Professor Brukhonenko pursued a series of researches first with isolated organs and later with total perfusions. At the third Congress of Physiologists of the U.S.S.R. on June 1, 1928, some of his experiments were demonstrated before an audience which included scientists from Britain.[5] Early in the next year a correspondent of *La Presse Médicale* who had paid a special visit to Moscow described these researches and published photographs of the apparatus in action.[6]

In his total perfusions Brukhonenko stopped inflating the lungs of the experimental animal and excluded its heart from the circulation by mechanical means. In three such experiments when he discontinued the perfusion and restarted pulmonary inflation he succeeded in restoring a temporarily effective heart-beat. He also observed that cooling of blood in the extracorporeal circuit reduced the temperature of the perfused animal, and to overcome this surrounded some of the tubing with warm water. In a paper submitted for publication on October 11, 1928, he used these words (translated from the original French):

> "Would not this method, duly perfected, be useful in clinical medicine; notably in those cases where it would be essential to replace, if only for a time, the work of the failing *human* heart? Without going more deeply into this question we can state as a result of the present work, that *in principle* artificial circulation is applicable to man not only clinically, but perhaps also for certain operations on the temporarily arrested heart. For its achievement, however, a suitable technique would have to be worked out." (The italics are in the original.) His summary ends: "The solution of the problem of the artificial circulation of the whole animal opens the door to the problem of operations on the heart, for example on the valves."[7]

Brukhonenko's work demonstrated the difficulties of total perfusion and went a long way towards resolving them. His technique of excluding the heart of the perfused animal from the circulation was crude, but was recognized as a

(*Continued at foot of next page*)

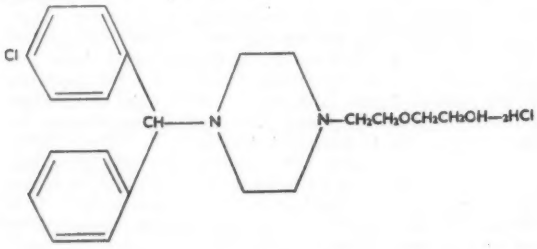
To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Hydroxyzine

" Atarax " (Harvey Pharmaceuticals).

Chemistry.—Hydroxyzine hydrochloride, like benactyzine, is a derivative of diphenylmethane. Its chemical name is 1-(*p*-chlorobenzhydryl-4-[2-(2-hydroxyethoxy) ethyl] piperazine dihydrochloride, and the structural formula is as follows:



Pharmacology.—Hydroxyzine is said to suppress autonomic overreactivity to stress, probably by depressing the reticular formation of the brain stem. It is said to help diminish states of tension and restlessness of psychogenic or organic origin.

Therapy.—The drug has been tried in the treatment of psychoneuroses, reactive depressions, psychosomatic conditions, premenstrual tension, emotional disorders of pregnancy, and menopausal states. It has also been given to diminish psychomotor restlessness and agitation in various senile conditions and in low-grade mental defectives. Recent trials[1–3] have failed to confirm earlier optimistic reports. Doses ranging from 10 to 100 mg. three times a day or more may be helpful in relieving mild symptoms of tension in some cases, but, as with benactyzine, amylobarbitone is often just as or more effective. Reactive depressive states and severe premenstrual tension respond better to the monoamine oxidase inhibitor group of drugs. Restless senile and presenile dements are usually better treated with a phenothiazine compound.

Contraindications.—None.

Toxic Effects.—These are rare and of little importance in doses of 25 mg. t.d.s. Sedative effects are minimal.

N.H.S. Basic Price.—10-mg. tabs., 100 for 26s. 4d.; 25-mg. tabs., 100 for 52s. 8d.; syrup, 4 fl. oz. for 8s. 4d.

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(*Continued from preceding page*)

method of achieving planned cardiac arrest. His writings were clear and precise in their prophetic insistence that this early work was applicable to the clinical needs of man.

W. R. PROBERT.
D. G. MELROSE.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Aphthous Ulcers

SIR,—We read with great interest the report (March 12, p. 764) by Mr. B. E. D. Cooke and Dr. P. Armitage on their double-blind, controlled clinical trial of mouth-tablets of hydrocortisone hemisuccinate sodium (" corlan pellets ") in the treatment of recurrent aphthous ulceration of the mouth. As we ourselves based our original report[1] purely on clinical judgment, we are naturally very pleased that other workers should put this form of treatment to a critical test.

However, there is one particular point in the study by Cooke and Armitage which seems to us to be of great interest and capable of a different interpretation from that given by the authors. They found that the difference between hydrocortisone and dummy treatments of eight weeks' duration was significantly less if the hydrocortisone were given before the dummy than if it were given after. This type of situation can be explained prima facie in one of three ways: (1) The drug is a long-acting one; or (2) the effect is psychosomatic; or (3) treatment carries a beneficial after-effect because it has broken a vicious circle in the progress of the disease at tissue level.

The first of these possibilities does not arise in the present case, because the small quantities of hydrocortisone contained in corlan pellets would be utilized by the body during the day of use, but the second and third possibilities are worth consideration. As far as psychosomatic effects are concerned, it seems to us that these are unlikely to have accounted for the difference to which we refer, because it is notable that, after four weeks when the patients received no treatment, putting them on to dummy tablets had no effect in reducing the extent of ulceration of the mouth. It therefore seems much more likely that the third possible explanation is the correct one—namely, that after two months' treatment with hydrocortisone some degree of resistance to aphthous ulceration is conferred on the mouth for the next few weeks. We are tempted to think that this is the correct explanation, because we have treated many patients with severe aphthous ulceration with daily use of four corlan pellets for much longer periods of time than two months and have observed that a considerable proportion of them will then be completely or almost completely relieved of aphthous ulceration for many months.—We are, etc.,

S. C. TRUELOVE.
R. M. MORRIS-OWEN.

Nuffield Department of Clinical Medicine,
The Radcliffe Infirmary,
Oxford.

REFERENCE

1 Truelove, S. C., and Morris-Owen, R. M., *Brit. med. J.*, 1958, **1**, 603.

SIR,—Aphthous ulceration of the mouth is usually a mild condition which may sometimes become very troublesome and give the patient much discomfort. The introduction by Truelove and Morris-Owen[1] of the local application of hydrocortisone hemisuccinate-sodium

tablets has been a great boon to the sufferers of this common, recurrent, annoying condition. It very seldom happens, however, that the condition becomes severe enough to assume serious proportions. The following is a description of such a case, in which after five months of suffering, the condition cleared up "miraculously" in a short time with the local application of hydrocortisone hemisuccinate.

A woman, aged 42, had suffered from aphthous ulceration of the mouth all her life, but the attacks had always been mild and transient. The present attack had lasted five months and was very severe. It started after the extraction of five teeth under local anaesthetic. (No antibiotics had been employed at that stage.) The mouth became affected with aphthous ulceration almost immediately after the removal of the teeth, the condition persisted, and it became progressively worse. About a month ago cultures of the mouth showed the presence of a mixed infection; repeated blood counts showed a mild hypochromic anaemia. She was given "tetrex" (a tetracycline phosphate complex) and chloramphenicol, vitamins by mouth and injection, and iron by injection. The mouth improved for a week or two, but after that it became much worse again. The mouth was very painful: the patient could not eat or talk, for the last five days she had lived on sips of milk, and she could not sleep at night because of the pain.

When she presented herself she was in a pitiable state and both she and her family were extremely worried and anxious. She could not speak at all, so had to answer all questions by writing on a pad. She could not swallow her saliva and was dribbling all the time. She could not open her mouth or move her tongue. On examination of the mouth there were many confluent aphthous ulcers on the gums, inside the lips and cheek, and on the under surface of the tongue. The dorsum of the tongue was thickly coated, but it was impossible to see if there were any ulcers on its surface because the patient could not put her tongue out. There was no bleeding of the mucosal surface. There was a small submaxillary gland in the neck. Apart from that, the history and the general examination proved to be negative.

The patient was given "corlan pellets" (each pellet contains hydrocortisone 2.5 mg.) and instructed to place one on the large ulcers three times a day. She was also given vitamin-B compound. The patient was first seen by me at 4 p.m. She applied the hydrocortisone pellets three times that day. By next morning there was a tremendous improvement and she could raise her tongue. The second day she applied the pellets three times and by next morning the last ulcer on the tongue had gone and the whole condition had cleared up and she did not apply the pellets any more. Thus, the condition took about thirty-six hours to heal. During that time she had a total of 25 pellets. After that she remained well and could eat normally. She thought it was a "miracle" that her mouth healed in time for her to enjoy the Christmas turkey. When I saw her two days later the mouth appeared normal, there was no sign of ulceration, and the dorsum of the tongue was clear. Menstruation had come on a week earlier than usual.

Truelove and Morris-Owen recommend a maximum dose of four tablets a day—that is, 10 mg. of hydrocortisone. This patient took 25 tablets in 36 hours—i.e., 62.5 mg., a very much larger dose. It was not intended that the patient should take so much, but there appeared to be no side-effects, unless it precipitated an earlier onset of menstruation.—I am, etc.,

Groote Schuur Hospital, Capetown, South Africa. LOUIS MIRVISH.

REFERENCE

[1] Truelove, S. C., and Morris-Owen, R. M., *Brit. med. J.*, 1958, 1, 603.

Diabetes in General Practice

SIR,—The article by Dr. I. H. Redhead on the incidence of diabetes in general practice (*Brit. med. J.*, March 5, p. 695) prompts us to mention a curious feature of the incidence of the disease in our own small mining-village practice with a list number of about 2,850.

We have 21 known diabetics on the list, and, of these, 11 live in a localized part of the village in two lanes off the main road within 400 yards of each other. In the first lane of five houses there are three diabetics, two of whom live next door to each other, the third living in the next house but one. In the second lane consisting of 22 houses there are four diabetics; two of these live next door to each other and a third in the next house but one; the fourth lives just opposite the latter. On the main road between the limits of these two lanes live four more diabetics, two of whom are father and son living next door to each other; the remaining two of the series live four doors away from each other. We also know of two patients in the next village who are diabetics and have been next-door neighbours for many years. The ages of these localized diabetics vary between 2 years and 74; all have been to diabetic clinics, and of these 11 only the youngest is a male.

One is very tempted to think that there is some very localized environmental factor at work here; we wonder if other doctors have similar diabetic "breeding-grounds" in their practices?—We are, etc.,

Garnant, Carms. F. I. POWELL. R. E. BLAIR.

Phenethyldiguanide

SIR,—Dr. Julius Pomeranze (*Journal*, February 6, p. 425) makes some interesting observations concerning our preliminary communication on phenethyldiguanide (D.B.I.) (*Journal*, November 14, p. 1005). He suggests that the ketosis occurring during D.B.I. therapy is due to "starvation." The fact that the blood-sugar readings were normal or somewhat elevated at the time, in our opinion disproves this; if, on the other hand, he uses "starvation" in the sense of the unavailability of glucose, then this is a toxic effect. It cannot be accepted that metabolic insult precipitated acidosis in our patients, as no such factor was found if it is allowed that moderate exercise should not constitute a danger.

Dr. Pomeranze suggests that increased blood lactate and pyruvate levels which have been observed in patients on D.B.I. are not sustained or cumulative and that they do not cause a reduction in alkali reserve. This is directly contradicted by work which we hope to publish soon.

While it is true that D.B.I. has not been proved to have a direct action in causing glycogen depletion, we agree with Dr. Pomeranze that the failure of D.B.I. to encourage glycogen synthesis results at least in a relative deficiency of glycogen as we have already suggested. In conclusion we disagree with the observation that even with careful biochemical control one should not encounter difficulties with any class of diabetic patient on D.B.I. Our experience indicates that juvenile diabetics with supplementary insulin are also liable to severe acidosis. The makers claim that "no histologic or functional changes in liver, blood, kidneys,

heart, or other organs were seen." The repeated finding of sustained high blood-lactate levels is in poor accord with this statement.—We are, etc.,

R. S. WALKER.
A. L. LINTON.

Law Hospital,
Carluke, Lanarkshire.

REFERENCE

[1] *Diabetes*, 1960, **9**, A-9.

Emotional Stress and Coronary Disease

SIR,—In your leading article on emotional stress and coronary disease (March 19, p. 866) you refer to Russek's publication[1] in which he stated 91 of 100 patients under 40 years old who developed coronary heart disease had severe emotional strain preceding the attack. May I point out that in my review[2] of 100 cases of coronary occlusion in young adults (all under 35 years of age) who served in the British Forces during the war years and developed coronary occlusion either during service or in civil life following discharge there was little evidence of any relationship to heavy responsibilities or mental stress ?

Only 9 out of the 100 cases were officers, and all of these, apart from a doctor and an instructor lieutenant in the Royal Navy, had begun their service as rankers. None of the commissioned officers were of higher rank than lieutenant and so would not have been subjected to heavy responsibilities. Most of the cases fell in the Registrar-General's social classes IV and V. There was only one female in the whole series, and even allowing for the greater number of males to females in the services—10–15 males to 1 female—there seems no doubt that coronary heart disease in the younger age groups is very rare in females.

The only other outstanding feature was the body build, the good physical development of these young adults ; most of the patients were above the average weight for age and height. What was remarkable was the very advanced degenerative changes in the coronary arteries found at necropsy in some of these young patients, indicating the pathological process had been present for years. These advanced pathological findings at such an early age, the preponderance in males, the body build, and the lack of relationship to mental stress or other extraneous factors support the view that genetic influences are the more important factors in the aetiology of coronary heart disease in young people than habits of life and work.

The literature on the pathogenesis of coronary heart disease is full of contradictory opinions, and there is barely one conclusion which has not been seriously challenged in recent months by workers of repute in the same fields. Even the increased incidence of coronary disease revealed by vital statistics has been called "largely artificial." In a recent review[3] the authors stated: "One (criticism) is that most of the studies have focused attention on the concentrations of serum cholesterol, serum lipid or serum lipoprotein, without proper emphasis on the focus of the problem, which is atheroma and infarction." In the present state of our knowledge the relationship of emotional stress and coronary disease must be considered as purely speculative, and, in spite of the enormous amount of work which has been done in recent years on the pathogenesis of coronary heart disease, the cause still remains unknown.—I am, etc.,

London, N.W.3. M. NEWMAN.

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[1] Russek, H. I., *J. Amer. med. Ass.*, 1959, **171**, 503.
[2] Newman, M., *Lancet*, 1951, **1**, 1045.
[3] Page, I. H., *Circulation*, 1957, **16**, 163. Quoted by Morgan, A. D., *Advances in Cardiology*, 1959, **2**, 255.

SIR,—I hope that I may be allowed to welcome your recent leading article on emotional stress and coronary disease (March 19, p. 866). Your general support for the suggestion that stress may play a part in causing coronary thrombosis (and possibly hypertension too[1]) is both timely and useful.

You make the point about comparing stress in different groups and nationalities. Such comparisons are inevitably very broad generalizations, because stress is, by definition, something which affects individuals and not groups. Stress is generally defined as being the internal or resisting force set up within the human organism by reaction with the environment. It is thus a function of failure to adapt successfully to a situation, or inability, often for subconscious reasons, to solve a frustrating problem. Unsolved problems are stressful ; solved problems, even if they involve hard work and fatigue, are morale-raising. Situations in which a whole community is under pressure tend to raise rather than to lower morale. This is because what may be stressful to an individual tends, when the whole group is involved, to bind it together and promote group solidarity. Wars, floods, and famines tend thus to promote group solidarity and to lower, rather than raise, the incidence of stress disorders. Stress is, in brief, one man against his environment. This is a possible reason why certain occupational groups, especially those in which there is a drive to get to the top or to do better than the other man, may show a higher incidence of stress diseases than would a group in which conformity is the general rule.

An additional point about coronary thrombosis which is not widely enough realized is that in what has been called "young man's coronary thrombosis"—which means roughly the under-fifties—the disease process is usually confined to the coronary vessels. In older people it is part of a generalized atherosclerosis involving the whole vascular tree and may be regarded more as an inevitable wear-and-tear condition. This was brought out by Yater *et al.*[2] and is further discussed in a forthcoming paper in *The Practitioner*.[3]

If I may be allowed to make one further point, it is to say that we are, in this unit, particularly concerned about the possible aetiological influence of both stress and environmental factors in coronary thrombosis. If these factors play a part in causation, it would seem likely that the negative advice which is so often given to a man who has had a coronary thrombosis while still in the prime of life may to some extent increase rather than diminish his load of frustration.—I am, etc.,

H. BERIC WRIGHT.

Medical Research Unit,
Institute of Directors,
London, S.W.1.

REFERENCES

[1] Hambling, J., in *Essential Hypertension: Modern Trends in Psychosomatic Medicine*, edited by D. O'Neill, 1955. Butterworth, London.
[2] Yater, W. M., Traum, A. H., Brown, W. G., Fitzgerald, R. P., Geisler, M. A., and Wilcox, B. B., *Amer. Heart J.*, 1948, **38**, 334.
[3] Wright, H. B., *Practitioner*, 1960. In press.

Tempo of Modern Life

SIR,—I was delighted to read in Dr. I. Atkin's article (*Journal*, December 26, 1959, p. 1477) the scorn with which he treated the theory that many of to-day's mental disorders were due to the "rapid tempo of modern life." Ever since I heard this phrase fall so frequently and so blandly from the lips of my medical teachers 10 years ago, I have been suspicious of it. As Dr. Atkin points out, life in England to-day is very much safer, securer, and more comfortable than it has ever been before.

If there has, in fact, been an increase in mental disorders in recent times, the cause, I think, lies elsewhere. It lies in the fact that in the days before the

Industrial Revolution, as opposed to nowadays, each man knew and accepted his lot. The son of a farm labourer seldom aspired to be other than his father, and the thought of becoming Prime Minister never entered his head. And so it was, on the whole, with artisans, fishermen, merchants, grocers, and everyone else. With few exceptions, a man was content to "fulfil his duty in that state of life into which it had pleased God to call him." There were not the strivings, the jostlings, the ambitions, the careerists, of modern times. To-day we are proud that there is freedom of opportunity for all. But what a price, in neuroses, alimentary derangements, cardiovascular diseases, and other stress disorders do we pay for it!—I am, etc.,

Lautoka, Fiji. S. R. S. LAING.

Progress in Psychiatry

SIR,—The review of Volume 3 of *Recent Progress in Psychiatry* (March 12, p. 787) contains a comment that "much too much space has been wasted on topics about which very little is really known at the present time," the "Enzymatic Basis of Certain Psychoses" and "The Psychiatry of Major Crime" being quoted as examples of such space-wastage.

It is with some trepidation that I venture to challenge the opinion of such a distinguished psychiatrist as Dr. William Sargant, but surely the purpose of the monographs, assembled in this volume, is to present to the reader the latest information, thought, and deductions on just those subjects on which admittedly so little is known. Descriptions of new treatments described as "often of a quite empirical nature," which the reviewer would have liked to see, are no stimulus to further advances, whereas the two papers mentioned, by pointing the way to a reasoned approach based on known physiological and biochemical premises, give positive guidance to those whose work takes them into the clinical fields of toxic psychoses and criminal behaviour. For my part, I found these papers unusually illuminating and I think many other readers will share this view.—I am, etc.,

London, W.13. AUDREY Z. BAKER.

Truth about Psycho-analysis

SIR,—Because Professor H. J. Eysenck, a distinguished psychologist of the conscious mind, has presumed unwittingly to rationalize his dislike of the psychology of the unconscious mind in the February edition of *Reader's Digest*, I seek the hospitality of your columns to reply.

Briefly, the gist of his diatribe was that there is no statistical proof that this prolonged and costly treatment of psychoneurotic illness offers any advantage as regards efficacy over the simpler more speedy methods of orthodox psychiatry and that therefore its continuance as a treatment has not yet been proved justifiable. One would like to inquire whether this writer has had any personal experience of treating psychoneurotics by the orthodox methods commonly employed in all progressive mental hospitals. I had over twenty-five years of such experience, but found, as many others have found, that they afforded temporary palliation only for the psychoneurotic. Since the critic is a conscious psychologist and not himself a psychiatrist, the probability is that he has had no personal experience at all, but has accepted what he prefers to believe.

My reply is as follows: It is true that no statistical proof of the superiority of the psycho-analytic method exists, but nor does statistical evidence of any reliable kind exist to the contrary, so that to quote statistics as a premise for condemnation is, I contend, quite unwarrantable. The statistical claims in support of the efficacy of the more popular palliative methods, one knows, are often fallacious. The aim of psycho-analysis is not merely one of temporarily securing a remission of symptoms, but of attaining permanent freedom from all further trouble. How far this is fulfilled depends, I submit, upon two main factors—namely, upon the competency of the analyst—and there are many incompetent ones especially to-day—and upon the suitability of the patient, by which one means his capacity to co-operate adequately and to continue with the treatment sufficiently long. I agree with the critic, however, that there is no possible justification for an analysis being allowed to drag on for years, thus merely adding penury to obviously ineffective treatment. One thinks nowadays in terms of months, not years. Surely the case quoted, in condemnation, was quite exceptional.

In conclusion I would quote words attributed to that great scientist and seeker after truth, even after unpopular truth, the late Sir William Crookes, F.R.S., who is alleged to have said: "He who seeks truth should be prepared to sit before it like a little child, prepared to follow wherever it may lead and to discard, if necessary, his most cherished preconceived notion." Alas, though, none is so blind as he who will not see, and perhaps the greatest enemy of truth is popular prejudice, which should not be encouraged.—I am, etc.,

Croydon, Surrey. WM. H. SHEPLEY.

Tests of Fitness to Drive

SIR,—With the increasing awareness of the need to avoid road accidents and their increasing toll of human life and suffering, greater interest appears to be taken in the question of fitness for driving, and the examiners who carry out the driving tests occasionally raise the question of fitness to drive at all, a question which the local authority may have to take up. In this they seek rightly the help of their psychiatric colleagues and of clinical psychologists.

It would appear to be desirable that some fairly standard testing procedure should be evolved so that a measure of uniformity of practice can be achieved; possibly a battery of tests (with the minimum of apparatus) might form the basis of an examination, although it is impossible to reproduce the factors involved in the actual driving situation. If any of our colleagues have made a special study of this problem and evolved a technique for dealing with it, a publication of their views would be of great interest.—I am, etc.,

Barrow Hospital, Near Bristol. A. LEITCH.

Accuracy of the "Breathalyser"

SIR,—There is one point which seems to have been overlooked in connexion with the possible use of the "breathalyser" on motorists. The conclusion reached by the B.M.A. Committee that "a concentration of 50 mg. alcohol in 100 ml. of blood while driving a motor vehicle is the highest that can be accepted as consistent with the safety of other road users" (*Brit. med. J.*, January 23, p. 269) was based largely on the results obtained by Professor G. C. Drew and his colleagues

based on direct analysis of blood-alcohol concentration.[1] No such conclusion could have been drawn from breathalyser tests, for the accuracy of the instrument is only ±25 mg./100 ml. at the 95% confidence limits. Thus, 50 mg./100 ml. reported by the breathalyser would represent values down to 25 mg./100 ml. in nearly half the subjects tested, while five in every 100 might be below 25 or above 75 mg./100 ml.

Opinion is divided as to the proportion of accidents which can be ascribed to alcohol, and, if the object of legislation is to make the roads safer, disqualification would seem to be the obvious penalty for dangerous driving, whatever its cause. If, on balance, alcohol is considered so important a contributory factor as to merit special attention and the breathalyser is to be used in its detection, a fixed limit of 50 mg./100 ml. is not practicable. Motorists must either forgo alcohol altogether and the instrument be used in a qualitative manner, or some higher fixed limit be set.—I am, etc.,

Department of Physiology, University College London, London, W.C.1. M. GRACE EGGLETON.

REFERENCE

[1] Drew, G. C., Colquhoun, W. P., and Long, H., *Brit. med. J.*, 1958, **2**, 993.

Alcohol and Road Accidents

SIR,—The terrifying loss of life on the roads is only slowly stirring the conscience of the public, and indeed of the medical profession also. The seeds of the problem lie in the nature of man. None of us is perfect, and one of the commonest and most dangerous of emotions is frustration. This so often leads to impatience, which in a road user may be fatal. Road improvements and new motorways will diminish obvious dangers, but will also increase the temptation to take risks to the limit of safety and beyond. It should follow without saying that judgment should be as unimpaired as possible. I therefore find disturbing the letter from Dr. Guy Roworth (February 6, p. 419), as he belittles the effect of alcohol on the number of road accidents. The peak incidence for road accidents is after the pubs have closed at night. As has been stated so often, it is not the grossly drunk driver who is the menace, but the one in whom overconfidence is engendered by a little alcohol.

Let us give wholehearted support to any measures which will lessen the toll of the roads. And if we cannot control the temperament of fellow drivers, let us at least attempt to control our own emotions. Doctors are often frustrated in their continual struggle to keep up to schedule, and the temptation to take risks is ever present. We must certainly look to ourselves.—I am, etc.,—

Wirral, Cheshire. J. GAVIN FOLEY.

SIR,—The recent B.M.A. booklet "Relation of Alcohol to Road Accidents" (January 23, p. 269) quotes on page 25 some figures which I published on urine-alcohol levels of drivers arrested for being under the influence of drink.[1] The booklet misrepresents in one small particular, however, the figures set out in the paper referred to; it says "that for those drivers definitely considered unfit to drive by clinical examination, the normal distribution was around a mean value of 300 mg./100 ml." In fact, the normal distribution around a mean of 300 mg./100 ml. applied to *all* the samples submitted to the Bristol Laboratory by police forces in the south-west. In a small number of cases, the subjects from whom these samples were taken had been medically examined and either certified fit to drive or had been put down as borderline cases (i.e., cases not definitely unfit). The proportion of subjects to which this applied was, of course, higher with small than with large urine-alcohol concentrations. Therefore the mean for all subjects clinically certified unfit would be slightly higher than 300 mg./100 ml. Unfortunately I am not now in a position to give the actual figure for this mean, since I no longer have access to the original records from which the figures were taken.—I am, etc.,

Newcastle upon Tyne, 3. H. J. WALLS, Director, Northern Forensic Science Laboratory.

REFERENCE

[1] Walls, H. J., *Brit. med. J.*, 1958, **1**, 1442.

Housing for the Old

SIR,—As a psychiatrist who claims only a fragmentary knowledge of social science, may I question the wisdom of the Birmingham Welfare Committee's plans (March 12, p. 816) for a multi-story home for old people, on Swedish lines? At first the idea of making provision for 76 old people in a modern building with all modern conveniences appeals enormously. On quiet reflection I am not so sure.

Can old people adapt to an environment of modern building materials, textures, and hygienic devices? Will it make the few years they have left more acceptable to be packed away from their community, however imposing the institution? I suspect that a majority would be more at home and happier living in the kind of house they have always lived in, in the area they have always known, surrounded by the photographs, bric-à-brac, furniture, and personal possessions they have acquired, with a kindly eye from a housekeeper of a similar background and, most important, not segregated from their community. These principles have been set out by the Abbeyfield Society, and seem to have proved successful over the last five years.

I do not mean to disparage what may be an excellent plan producing first-class results. I would like to draw attention to the need for a scientific evaluation of the effects—intellectual, emotional, and social—of the project. Would it be impertinent to suggest that 5% of the capital outlay be provided for such an investigation: to find out if it is worth while, to tell us if we are going in the right direction?—I am, etc.,

Severalls Hospital, Colchester, Essex. RUSSELL BARTON.

Shoes for Children

SIR,—We hear from time to time of foot and shoe surveys sponsored by public-health departments, and the Ministry of Health has just promised us another, privately financed (by the shoe-trade?). From Mr. T. T. Stamm's description in *The Times* it looks like being as fantastical and delusive as the rest, if what one dreams of is an improvement in the mutilation going on *now* in children's and adults' feet, especially women's.

Why cannot people grasp the problems that are there? Dr. Catharine Hollman, in her lengthy article (March 5, p. 719), writes of visiting shops with a "foot health nurse" to check on the availability of "well-shaped" shoes for children, "that is, [shoes] with rounded toe and a straight inner border." Does she not know that a round-toed shoe, *tout simple*, may be an even greater hazard than a pointed-toe? With a pointed toe it is possible to insist on the point being opposite the big toe, longest and thickest member of the forefoot and key

organ in locomotion (as in deformity): with a rounded toe it is almost inevitable that the terminal phalanx of the great toe is caught by the rounding and displaced towards the centre of the shoe, the first and irrecoverable stage in the creation of a hallux valgus. With a straight inner border—if she means what she says—the natural swing of the forefoot inwards is ignored and made impossible in all the activities of children which typically involve raising the heel off the ground (as in tripping, climbing, dancing, running) and accentuating the degree of swing present when the foot is at rest. The axes of the heel and forefoot meet at an angle: that is, the borders of the two together are neither "straight" nor parallel, and the foot forced into a shoe with a straight inner border is having its fore part displaced into the valgus position and the inner longitudinal arch strained at its weakest point—i.e., the nominal keystone, where the immediate support of the superincumbent structures is a soft tissue—namely, the inferior calcaneo-navicular ligament. Result, traumatic flatfoot, without any lower age-limit in the walking period, if "straight" shoes are worn.

Let the inner shoe border be straight from the ball till it clears the big toe, by all means. It can, with advantage, while straight veer slightly in. Then let its junction with the anterior border of the shoe (which it meets at something less than a right angle) be rounded off: that is common sense. But no "rounded toe." If the shoe is thus well-shaped it must be fitted to the foot, for length and for width. In all her search for up to "four width-fittings" Dr. Hollman does not tell us if she met or searched for adequate foot-measuring instruments, or, if she found them in conjunction with her "four width-fittings," whether they were used. What's all the rest, without that?—I am, etc.,

London, S.W. MARGARET EMSLIE.

SIR,—I have read Dr. Catharine Hollman's article on children's shoes (March 5, p. 719) with great interest. It is a matter to which I have given some thought, and the problem seems insoluble. The older the child (I am referring to girls), the more difficult it becomes. We all know the advantages to be gained from wearing sensible shoes, but—let me be quite dogmatic about this—straight inner margins and rounded toes mean ugly footwear, and no amount of medical prating will persuade shops to stock them or teenagers to buy them. I see little wrong with the low-heeled casual shoe—the "flattie," but the stiletto-heeled, pointed court is a horror by any standard.

Do we, perhaps, blame our shoes too much? Some members of my family, including myself, are bedevilled with narrow feet and a high dorsal arch which make the buying of well-fitting shoes expensive and frustrating for the adults and wellnigh impossible for the children. Perhaps the trouble lies within ourselves and it is the deformed gene rather than the ill-fitting shoe which leads to the deformed foot. "Choose your parents well" would seem to be as true of feet as of much else in life.—I am, etc.,

Nottingham. CATHERINE SWANSTON.

SIR,—I would like to congratulate Dr. Catharine Hollman on her article "Shoes for Children" (March 5, p. 719). I was very glad that she agrees that the casual-type of shoe can only stay on if too short. I was, however, a little doubtful if her criterion for a good shoe—namely, "well-shaped"—was adequate. What about the weight of the shoe? Many children's shoes are very heavy, with a heavy heel and unyielding sole, with the result that they encourage out-toeing and an incorrect posture when standing. A child cannot walk with a proper foot action if the sole will not bend, but only "homeward plod his weary way."

As regards fittings of children's shoes, would it not be interesting to find out how many shops measure the real length of the foot—that is, standing with full weight on it? Also how many measure both feet?—I am, etc.,

Tunbridge Wells. W. H. GERVIS.

SIR,—Mr. J. Anthony Clark (March 12, p. 803) is quick to take up his pen in support of the work done by his firm in promoting adequate footwear for children. But we would be more impressed if he showed the same concern about footwear for teenagers and adults. Why is it assumed that it is only in the growing period that foot faults will occur? Why must we confine our education to parents and give the impression that it is only during the growing period that we have to take care of the feet? The problem is a much wider one. As Mr. M. D. England points out (p. 803), the only sensible shoes are those held on by lace, strap, or elastic across the dorsum of the foot. All the rest—the casuals, the courts, and the slipper types of footwear which fill our shops—are orthopaedic abominations and harmful at any age. There are only two ways of keeping on such footwear. Either the shoe is so short that the forefoot is jammed into it, or, if it is of adequate length, the wearer has to curl up her toes in order to prevent the shoe from falling off.

Anyone going round the average small town will find it almost impossible to buy a sensible smart shoe for her teenage daughter or for herself. Why? Because such shoes are not fashionable, and are therefore not made. No doubt Mr. Clark and his fellow manufacturers say that they can do nothing about altering the fashion. That may be so, but we have seen no real effort on their part to influence taste in teenage and adult footwear. The fact remains that it is fashionable, and no doubt profitable to the manufacturers, to wax eloquent about the importance of adequate juvenile footwear, and the importance of protecting the child from deformities of the feet, but it is considered bad taste to spoil the self-expression of the teenager who wants to be smart.

May I suggest a constructive step towards better footwear for the nation? Let the manufacturers get together and advertise in the same way as the Milk and Egg Marketing Boards. Let them produce educational advertisements describing the principles of good footwear which apply to all age-groups, and let them back up this campaign by producing sensible and smart shoes for all age-groups.—I am, etc.,

Bridgend General Hospital, Glamorgan. A. W. FOWLER.

SIR,—The "bulge" age-group of girls in the secondary schools often need shoes of size 6 and over. The girls like pretty light shoes and therefore wear casuals, and only the firmest parents succeed in making them wear lace-up shoes or bar shoes, which are heavily built and *are* available.

I should like to ask where are the pretty light shoes conforming to Mr. M. D. England's requirements (March 12, p. 803). If any can be found they will be in ladies' shoes at £3 or over. Regarding the letter from the sales director of C. & J. Clark Ltd. (March 12, p. 803), I cannot find a pretty, leather, bar shoe in a *wide* fitting in size 6.

One maker has a pretty, light, bar shoe only up to size 5½, another maker in a March, 1960, catalogue has a size 6 light bar shoe, but this is *not obtainable till May* and *not* in a wide fitting. A brown lace-up shoe size 6 not heavily built was ordered in December and is not yet in the retailer's shop.

The mothers of adolescent girls should not be blamed for not making them wear suitable (light, reasonably priced, and pretty) shoes when such shoes *do not exist*. —I am, etc.,

Sanderstead, Surrey. EVE STRATON.

Speech Therapy and Child Guidance

SIR,—Recent developments in the Midlands have brought to the fore the problem of how the work of the speech therapist should be related to the team-work within or close to the clinic building. The good will of has to treat children with various organic disorders of verbal communication such as rhinophonia, dysphonia, dysarthria, and dysphasia, or with psychogenic disturbances such as stammering, dyslalia, and delayed onset of speech. No matter what disorder has been diagnosed the emotional basis or superstructure has to guide specialized treatment. The importance of diagnosis, for treatment proper—i.e., the testing of the diagnosis—is obvious. Since the speech therapist is expected to resolve the emotional difficulties of children with psychogenic speech disorders she ought to be working in association with the child-guidance team so that she may get information regarding the child's intelligence and emotional attitude and may administer psychotherapy or play therapy.

This brings up the question of training. Usually only the child psychotherapist (play therapist) is regarded as competent in this method of treatment. Not only has the speech therapist not graduated to the accepted status, but she is also faced with another adverse condition which accentuates the difficulties in that, working alone, she is denied the assistance of the psychiatric social worker who helps the mother to adjust her attitude to the child's problems. Some speech therapists do excellent work by using play therapy and by adopting also the role of the P.S.W. Yet there is a risk that others will fall down in this province. It might therefore be argued that speech therapists not conversant with the principles of play therapy should not treat speech disorders involving emotional problems. But the fact is that they do, and will continue to treat them with greater or lesser technical skill by interpreting the child's emotions expressed in his playing, drawing, and painting.

We suggest that: (1) The speech therapist should have the opportunity to work in co-operation with the child-guidance team so that their respective resources could be pooled. (2) Some arrangements should be made which would enable speech therapists to attain competence in play therapy, competence which many with an excellent standard of personality already possess. Until such time as provision is made in the training schools to equip speech therapists adequately for the work of play therapy and with a view to achieving our second recommendation for speech therapists already in practice, the child psychiatrist's co-operation would be helpful. Consultations and case conferences might take place between the speech therapist and the child-guidance team. That many speech therapists are working right away from any child-guidance clinic is no reason for not making a beginning where the speech therapist works within or close to the clinic building. The good will of directors of education and medical officers of health, no less than that of the speech therapists and the child psychiatrists themselves, would be essential for the smooth working of such a scheme.—We are, etc.,

DAVID T. MACLAY.
STELLA E. MASON.
LEOPOLD STEIN.

Uffculme Clinic,
Birmingham, 13.

Coincidence ?

SIR,—Do you ever see the I.T.V. programme "Emergency Ward 10"? On Wednesday March 16, one of our hospital secretaries told me that she had seen an instalment of this programme on the previous evening which to her seemed unusually familiar. This related to a young man admitted to hospital suffering from the effects of a serious overdosage of barbiturates and whose condition steadily deteriorated. He was given artificial respiration by a mechanical pump because of depressed respiration, and an infusion of noradrenaline because his blood-pressure fell profoundly. He continued to give cause for alarm, and it was eventually decided to try to dialyse some of the barbiturate, by now identified as butobarbitone, from the blood, using an artificial kidney. Tuesday's programme ended with the news that the artificial kidney was on its way to the hospital by road and would be in action in the next instalment, to be screened on Friday. Her interest in this programme was the more aroused because, a few months previously, she had typed out a script which seemed to be identical in every detail. This, Sir, you published in this journal under the title "Artificial Respiration and an Artificial Kidney for Severe Barbiturate Poisoning" under the authorship of Group Captain R. C. Jackson and myself (November 28, p. 1134).

My interest and curiosity were stimulated, and I was determined to see the next episode, and on Friday, March 18, I installed myself in front of my neighbour's television set. From the beginning, I felt that I had seen this saga before. It was a fairly accurate presentation of the events as related in our paper. The script itself followed the paper extremely closely, one might almost say word for word. The blood barbiturate levels as butobarbitone, before and after haemodialysis, were identical and so were the time relationships. The patient's response to dialysis, the state of his pupils, response to painful stimulation, and the measurements of tidal air volume, temperature, and blood-pressure were all faithfully reproduced. A graph showing the level of barbiturate in the blood at various times was shown in close-up on the television screen, and this seemed to be identical with the first part of Fig. 2 in our paper. The programme closed with the stopping of haemodialysis, and we now have to wait until Tuesday next to see whether the patient in the "Oxbridge General Hospital" continues to follow the same course as that of the man admitted to the Radcliffe Infirmary in Oxford. I rather think he might. Sir, is there not a copyright in the papers published in your journal?

I see from the advertised programme (*T.V. Times*, March 11, pp. 28 and 34) that the two scripts were written by Diana Morgan and Michael Ashe from an original idea by Tessa Diamond. Whose idea?—I am, etc.,

The Radcliffe Infirmary, Oxford. GERALD E. HONEY.

Asepsis on T.V.

SIR,—I was interested to read Dr. C. M. Ottley's letter (March 5, p. 728). In the B.B.C. television programme at 9.15 p.m. on March 8 they showed an excellent feature on immunization which was marred by one glaring mistake—the doctor blowing the smallpox vaccine lymph from the capillary tube on to the prepared area by means of his mouth. With the numerous rubber blowers available to-day this careless practice is quite uncalled for.—I am, etc.,

Public Health Department, Solihull. IAN MCLACHLAN.

SIR,—Professor Thomas Anderson (March 19, p. 882) deserves full support for his suggestion that it is time we reviewed the whole detail of the practice of immunization. There should be one basic rule: a separate, clean, sterile syringe and needle for each patient. This opinion is supported by the Medical Research Council,[1] a group of international experts on immunization,[2 3] and the good example of the public-health authorities in Manchester.

It is high time that all other commoner practices, with their unmeasured risk of inoculation hepatitis, were firmly declared by doctors to be indefensible—in every sense. If we cannot learn this lesson for ourselves I hope that we shall not complain when our patients at last discover how easily, and profitably, they can become our teachers in this elementary matter of public health. We should not expect that people will indefinitely tolerate our inflicting upon an unknown proportion of inoculees (in the name of preventive medicine !) a disease that can be fatal. To explain such conduct we could plead only ignorance, indifference, or poverty —and I mean poverty of spirit and outlook rather than of cash.—I am, etc.,

Department of Bacteriology, University of Glasgow. J. W. HOWIE.

REFERENCES

[1] *Mon. Bull. Minist. Hlth Lab. Serv.*, 1960, **19**, 26.
[2] *Brit. med. J.*, 1959, **1**, 1342.
[3] *Proc. Symposium on Immunization in Childhood, 1959*, 1960. E. and S. Livingstone, Edinburgh.

SIR, — Professor Thomas Anderson's criticism (March 19, p. 882) of the practice of blowing out lymph from the capillary tube by the mouth prompts me to describe a very simple and, I believe, safe method I thought of several years ago and have used ever since.

Into a clean dry 1 or 2 ml. syringe, fitted with a hypodermic needle (a No. 16 Record is suitable), draw about 1 ml. of air. Holding the syringe in the right hand and the opened capillary tube in the left, insert the point of the needle a few mm. into one end of the tube, not so far, however, as to allow it to come into contact with the lymph. Hold the tube and needle together by the thumb and forefinger of the left hand (thus virtually sealing the union), depress the plunger of the syringe fairly sharply, and the lymph emerges safely through the distal end of the tube, which should be held a short distance (say, 0.5 to 1 cm.) away from the prepared area of skin.—I am, etc.,

Horsham, Sussex. F. TAYLOR.

SIR,—Professor Thomas Anderson is right in his criticism of the recent B.B.C. Television programme on immunization with which we were both concerned (March 19, p. 882). To blow vaccine lymph on to a baby's arm with the mouth instead of with a teat must carry some risk of infection, but it is the technique used by many, if not the majority, of doctors who do smallpox vaccination in this country. We suspect that the vaccinator is more at risk than the vaccinated. Has Professor Anderson any figures to support his theory that the mouth technique does actually lead to more frequent secondary infection after vaccination than the teat technique ? We are, anyway, pleased that this lapse in the programme may have served a useful purpose in drawing attention to a widespread practice which might well be condemned.

We would like to know whether your printing of a doctor's name in connexion with this programme indicates that the *B.M.J.* no longer supports those of us who try to remain anonymous in television programmes. Since we still prefer to adhere to the principles advocated by the B.M.A. Ethical Committee, we hope you will allow us to sign ourselves:

A GENERAL PRACTITIONER.
A CONSULTANT PHYSICIAN.

*** It was not we but Professor Anderson who named one of the compères of the programme. Evidently a well-known face speaks for itself.—ED., *B.M.J.*

Chemotherapy for Cancer by Perfusion

SIR,—As an addendum to my report (*Brit. med. J.*, March 26, p. 952), your readers might like to know that when I was in Houston, Texas, in December, 135 perfusions had been performed there with only 2 deaths. —I am, etc.,

London, W.1. A. LAWRENCE ABEL.

Steroids and Steatorrhoea

SIR,—Dr. J. S. Jenkins in his letter (March 12, p. 800) regarding my article " Anterior Pituitary Deficiency in Disorders associated with Steatorrhoea " (February 20, p. 529) is correct when he states that both the plasma 17-hydroxycorticoid and urinary 17-ketogenic steroid levels should be determined in order to assess adrenocortical function. It is, however, difficult to explain such low urinary 17-ketosteroid values and their prompt responses to corticotrophin in my patients on any basis other than a state of anterior pituitary-adrenal insufficiency. Dr. Jenkins is fortunate to have the facilities for estimating plasma steroid levels, but he appears to be less fortunate in his supply of clinical material, for he has investigated adrenal function in only one patient with steatorrhoea. While he denounces, in vigorous terms, my conclusions drawn from so small a series as seven cases, he emphasizes his own unique experience.

I was aware that normal resting plasma steroid levels had been reported in patients with steatorrhoea and that these levels showed a normal response to corticotrophin. My suggestion that steatorrhoea may be associated with secondary adrenal *insufficiency*, and symptoms of such, is not incompatible with these findings. Indeed, it was with this knowledge that I deliberately used the term *insufficiency* to indicate that, despite apparently " normal " adrenocortical activity, the supply of circulating adrenal hormones could nevertheless be inadequate to meet demands. This point I made clear when I stated " . . . symptoms and signs of corticoid deficiency would depend upon the residue of steroids available for vital activities elsewhere after a variable proportion has been utilized in attempting to correct deficient absorption." The importance of this discrepancy between adrenocortical supply and demand was exposed and

accentuated in the patients I described because each had an *absolute* adrenocortical deficiency due to adenohypophysial insufficiency.

Dr. Jenkins states that the association between pigmentation and hypopituitarism is "extremely rare." If by this he means *organic* hypopituitarism I would agree that the association is uncommon; the condition I described was a state of *functional* anterior pituitary insufficiency. I had no reason to doubt the integrity of the intermediate- or the posterior-lobe; indeed, I held that the continued activity of the latter was partly responsible for the delayed water excretion. Certainly I intended to imply the preservation of melanocyte-stimulating hormone as the cause of pigmentation in these subjects, and my evidence for this view is to be published.

I also stressed in my article that, although others had considered that steatorrhoea might be associated with decreased anterior pituitary activity, they had attributed this to malnutrition—a condition which was not present in my patients. I made no claim that anterior pituitary insufficiency was the primary cause of steatorrhoea, but I would claim that any condition which persistently impairs intestinal function, and therefore provokes continuous pituitary–adrenal activity, will ultimately induce anterior pituitary exhaustion. Thus many of the features associated with steatorrhoea may not be due to the primary disorder *per se* but to the endocrine deficiencies which this disorder may provoke, and, furthermore, these deficiencies may themselves favour continuation of the primary intestinal lesion. This view would remove the difficulty of accounting for impaired water and carbohydrate absorption in steatorrhoea due to tuberculous enteritis; it would also explain the remission which occurs when patients with tropical sprue are removed to a temperate climate; and it might also account for coeliac dwarfism.

Though Dr. Jenkins would dismiss the concept of "anterior pituitary exhaustion" as a myth, it does help to explain certain clinical observations and reliable biochemical facts for which there is no other explanation at present. Far from "clouding the issue," this hypothesis, by discriminating between the features of the primary intestinal lesion and those of its secondary endocrine disturbance, would help to clarify the pathogenesis of the malabsorption syndrome.—I am, etc.,

Charing Cross Hospital, London, W.C.2. J. N. MICKERSON.

"A Case of Juvenile Cirrhosis"

SIR,—I have read with much interest the clinicopathological conference on "A Case of Juvenile Cirrhosis" (February 27, p. 631), and a few of the points that were discussed there confused me. Regarding mental deterioration, the few patients whom I have seen had not only the "fatuous facial appearance" but a true low I.Q. with some amount of dementia. I think ganglion-cell degeneration with neurological outgrowth in cerebral cortex may explain this. I think the advantage of penicillamine over B.A.L. (dimercaprol) is underestimated. Not only can it be given orally, but while it is being absorbed through intestine it can prevent absorption of copper, and thus makes the simultaneous administration of potassium sulphide quite unnecessary.

I was surprised to read Professor Sheila Sherlock's statement that administration of ceruloplasmin in classical cases of Wilson's disease is of no "clinical benefit." If it is true, our limited knowledge about this disease will need reorientation. Finally, aminoaciduria in these patients was explained by "copper poisoning of proximal tubules." But it is known beyond doubt that non-symptomatic relatives of the patient also have aminoaciduria, a fact which proves that kidney defect must also be inherited, which "copper poisoning" might aggravate, but the latter cannot be the sole offending agent.—I am, etc.,

Neurological Unit, Northern General Hospital, Edinburgh, 5. ANUPAM DAS GUPTA.

"Imferon"

SIR,—I would like to object strongly to your presentation of the leading article (March 12, p. 788) on the "Carcinogenic Risks of Iron-Dextran" that achieved some popularity in the general press. In compiling this, its author had obviously had considerable access to the literature quoted on this subject. It is unfortunate, therefore, that more detailed information could not have been supplied to your readers, with especial reference to the dosages employed (both daily and absolute) and their equivalents in man. Without such information the article has many illogical features.

The subcutaneous method of administration used by Haddow and Horning is not the usually recommended route. It is admitted that *massive* doses were used, and that each injection introduced an amount of iron that was several times the body content; and this also would appear to be a departure from normal routine. In these circumstances, without the aid of more detailed facts, one can but conclude that this carcinogenic response occurs only to mammoth absolute quantities.

The prescription and administration of this compound are under the complete control of the physician; it is not open to abuse by the general public, and is usually administered for short periods only. Massive dosage of any drug is dangerous. I cannot but help feel that a more helpful approach would have been to have advised us on the toxic limits involved rather than advocate the complete withdrawal of this drug.—I am, etc.,

Public Health Department, Dudley. D. KLEE.

SIR,—In your leading article (*Brit. med. J.*, March 12, p. 788) you pointed out the risks of treatment with iron-dextran in view of its carcinogenic effect in experimental animals. This has already caused a lot of sensation among the medical profession; it has also been brought to public notice in the *Guardian* of March 11. I think it is too early to ventilate this news publicly when it is not yet established that a similar carcinogenic effect has been observed in human beings. Considering the vast number of people who have been on this treatment the extent of excitement and panic amongst the lay public can be well appreciated.

As there is a cancer-susceptible strain of mice with a great tendency to develop spontaneous leukaemia, mammary cancer, and malignant tumours on other parts of the body, the effect of iron-dextran as a carcinogenic agent as worked out in mice and rats is rather questionable. Moreover, the total dosage needed to produce cancer in rats is hardly ever required in man to produce the desired therapeutic response. Considering the great therapeutic value of "imferon" in elderly people with iron-deficiency anaemia as well as in patients with rheumatoid arthritis and the malabsorption syndrome, should this experimental evidence still warrant the drug's withdrawal from general use?—I am, etc.,

Kingston General Hospital, Hull. B. K. KHASTAGIR.

Internal Tampons

SIR,—I was staggered at Dr. W. R. E. Harrison's wholesale condemnation of internal tampons (*Brit. med. J.*, March 5, p. 729).

I have always understood that there were no gynaecological contraindications to tampons used by normal healthy women and girls. With a normal flow, a tampon provides adequate absorption, and when saturated, if not removed, the flow leaks past, proving that drainage is in no way impeded. I feel that tampons are a tremendous advantage to women for many reasons, including comfort, ease of carrying spares and of disposal, and for the psychological advantages which far outweigh any disadvantages.

It is inevitable that an occasional woman will forget and leave one in, but in six years of practice I have never seen a case—nor, as Dr. Hypher suggests (March 5, p. 729)—do I think I've missed one. A gynaecologist tells me that he has only seen one case in his practice.

Has Dr. Harrison really discussed this subject with his patients and asked any who have used tampons for any length of time if they would like to return to towels? I think he'd find that they would be horrified at the idea.—I am, etc.,

Durham. SYLVIA A. MOSS.

SIR,—As a surgeon with only general principles to guide him, I was amused by Dr. Paula Gosling's letter (March 19, p. 879), with its reference to gauze packs for drainage.

Is drainage the purpose for which she advises tampons? I am reminded of a surgeon who at an important meeting between the wars showed a case which had suffered from temporo-sphenoidal brain abscess, and described how he had packed off the meninges with gauze to prevent them becoming infected and had then used a pack of the same gauze to "drain" the abscess. He seemed surprised that the patient had lived, a surprise shared by others.

I think it was Mr. Cozens Bailey who used to say at Bart's: "If you want to put in a plug, put in a plug. If you want to put in a drain, put in a drain. But don't have anything to do with that bloody gauze."—I am, etc.,

Okehampton, Devon. E. BROUGHTON BARNES.

SIR,—Removing a forgotten internal tampon can be a most unpleasant experience for the doctor, but I have never seen the patient suffer anything more serious than the temporary discharge. Has any case of salpingitis or tubo-ovarian abscess due to a neglected tampon been described? Dr. N. C. Hypher (March 5, p. 729) suggests it may occur. Nor do I agree with Dr. W. R. E. Harrison (p. 729) that the abuse of the internal tampon by a few is sufficient reason for depriving millions of women of the comfort and advantages of using them.—I am, etc.,

Witney, Oxon. MARGARET B. NOBLE.

Glycyrrhetinic Acid

SIR,—For some years you have accepted controversial reports on the merits of glycyrrhetinic acid as a local application in the treatment of skin diseases. When this correspondence was at its height (1956–7), I thought it would be of interest to investigate the part played by the two main active isomers of this acid, and I should be grateful if you would publish my results.

Four creams of identical base were used, and during the investigation their composition was known only to the manufacturers. Furthermore, they were dispensed at random by the pharmacist, and he alone knew which sample the patient received. *Cream A*—2% glycyrrhetinic acid in cream base, 24 samples used. *Cream D*—cream base alone, 23 samples used. *Cream K*—2% 18-a isomer in cream base, 21 samples used. *Cream S*—2% 18-b isomer in cream base, 20 samples used.

Eighty-eight trials were undertaken in eczematous and pruritic skin conditions which had been present for over three months and which do not normally fluctuate within the period of three weeks. In the cases under trial no other change of treatment, such as sedatives, etc., was allowed, so that the skin changes noted were presumably due to the application. Intelligent patients (and parents) were chosen, and in none was there a pronounced psychogenic overlay. The samples were given without enthusiasm with the advice that they should be applied twice daily. They were introduced as a new cream under clinical trial, which might prove to be more beneficial or less beneficial than the patient's previous local application. The cases were grouped from a clinical viewpoint as follows: Besnier's prurigo—mostly children and young adults, 42 cases; infantile eczemas of the atopic type, 22 cases; disseminated neurodermatitis, 17 cases; localized neurodermatitis, 4 cases; prurigo nodularis, 2 cases; and contact dermatitis (nickel), 1 case.

The results were recorded by figures estimating both the patients' reactions and also the clinical changes observed. It was found that creams K and S were equally much more anti-pruritic than creams A and D, and fewer patients found them irritating. Clinical observation, however, showed that cream S gave the best results, with creams K and D almost as effective; and all three were much superior to cream A, which contained 2% glycyrrhetinic acid. The pharmaceutical firm who kindly supplied these creams did not feel that these results merited further investigation. Last month I inquired from a firm which manufactures skin preparations of glycyrrhetinic acid if any work had been done in comparing the active isomers. The absence of a positive answer from that firm has prompted this letter.—I am, etc.,

London, W.1. IAN MARTIN-SCOTT.

Severe Tetanus

SIR,—I was very interested in the article by Mr. S. M. A. Alhady and his colleagues (*Journal*, February 20, p. 540). In view of their suggestion that tetanus toxin may have a direct effect on the myocardium, I thought it would be worth while mentioning a case that I treated four years ago.

A woman aged 60 was brought in to the casualty department complaining of trismus and generalized muscular stiffness. A diagnosis of tetanus was made although there was no history of trauma.

On the way to the ward she went into a generalized tetanic spasm, which was treated with paraldehyde. It was decided to place her on treatment with paraldehyde and mephenesin, rather than complete relaxants, and she was treated with paraldehyde and mephenesin at three-hourly intervals, plus antibiotics, plus large doses of antitetanic serum. The spasms were able to be controlled by this method and she was able to be fed by a gastric tube and the airway was managed to be maintained quite adequately without tracheotomy.

After a fortnight's therapy the spasms gradually abated and medication was discontinued. Two or three days after the cessation of therapy she suddenly died. At necropsy the only significant finding was acute heart failure with a

flabby atonic pale myocardium, which microscopically showed evidence of myocarditis.

I can think of no other reason why she should have developed myocarditis other than by the direct effect of the tetanus toxin, and this case bears some relation to Case 7 of Alhady *et al.*, and is also similar to the case described by Lassen *et al.*[1] in which an acute toxic myocarditis was found. It may well be that by keeping alive the inevitably fatal cases the effects of tetanus toxin on the myocardium may become apparent, whereas hitherto, with earlier death, they were not sufficiently advanced to be noticed. This question appears to warrant further investigation.—I am, etc.,

Southmead Hospital, Westbury-on-Trym, Bristol. S. G. FLAVELL MATTS.

REFERENCE

[1] Lassen, H. C. A., Bjørneboe, M., Ibsen, B., and Neukirch, F., *Lancet*, 1954, 2, 1040.

Barbiturate Deaths

SIR,—I would like to endorse Dr. D. T. Heffernan's comments (*Journal*, February 13, p. 503) on combined capsules of bemegride and barbiturates by quoting the case of a patient well known to me as a barbiturate addict.

This man was taking some 400 mg. and upwards of quinalbarbitone daily and was having increasingly frequent episodes of deep coma from overdose. This was without suicidal intention. I prescribed a combined capsule of quinalbarbitone sodium, phenobarbitone, and megimide (available under the name "phenaglate") in the hope of preventing this. However, his consumption of these capsules increased steadily to some 10 per day until he finally took a dose of 50 capsules. He may in fact have taken more than this, but my detailed investigation shows that this was the minimum quantity which could be accounted for. When seen some four hours after taking the capsules the patient was in a state of acute mental confusion, but without either drowsiness or respiratory depression. Later investigation revealed that he had taken the combined capsules in addition to his continued daily dose of quinalbarbitone which he had previously hoarded.

From my experience of this patient and others I would comment: (1) The combined capsules do not cause deep coma even in large overdose, which would have certainly produced coma if "plain" barbiturate alone had been taken. (2) In this case the analeptic effects of the bemegride predominated in the dose taken. In my opinion the combined capsules are unsuitable for barbiturate addicts because of this, and because I believe that tolerance to the barbiturates is increased by "megimation." (3) The value of bemegride in treating barbiturate poisoning is closely related to the time interval elapsing prior to its administration. The optimal effect occurs when barbiturate and bemegride are taken simultaneously as in the combined capsules. This time relationship, I feel, merits further investigation and would be an important factor to consider in any controlled study of the treatment of barbiturate poisoning.—I am, etc.,

London, S.W.15. J. K. SKINNER.

Methylated Ether and Convector Heaters

SIR,—May I beg the hospitality of your columns to record an apparently little-known matter of some interest to medical and scientific personnel working with methylated ether in rooms heated by electric convector heaters? Both my hospital clinic room and my private consulting-room are small, well-ventilated rooms; both are heated by electric convector heaters. It is my practice to use a "dab" of "ether meth." to cleanse the skin before vein puncture, but after one, or at the most two, such applications a peculiar acrid smell pervades the rooms and is of sufficient intensity to warrant the heater being turned off.

No one with whom I discussed the matter knows how the odour was produced. On the advice of the makers of the heater I wrote to Dr. J. H. Burgoyne, of the Imperial College of Science and Technology in London, and was informed that without doubt the trouble was due to the formation of aldehydes by the low-temperature (flameless) combustion of traces of ether-meth. vapour drawn into and passing over the heat element of the convector heater. The particular heater that I was using operates at a comparatively high temperature (600–700° C.—i.e., dull red heat), and this heat, I am informed, is rather higher than that in other types of convector heaters. Obviously a lower element temperature would produce an odour less noticeable or perhaps none at all. Dr. Burgoyne also mentioned that of course the presence of aldehydes in the atmosphere constituted a long-range warning of ignition, particularly if through accidental spillage a great deal of ether-meth. vapour was liberated into the air. It seems to me that, with the widespread use of convector heaters in consulting-rooms and laboratories, this problem may well be an increasing potential or actual nuisance, even a danger, and the facts should be more widely known.—I am, etc.,

Stamford, Lincs. JEFFERY C. SPRY-LEVERTON.

First Aid

SIR,—We were glad to see General F. C. Hilton-Sergeant's letter (March 19, p. 882). We endorse all he says, but in particular would like to stress the growing importance of first aid in industry. With the introduction of new legislation there will be an ever-increasing demand for first-aid classes during the afternoons, and any help which the medical profession can give with these important courses will be much appreciated. We already receive the most wonderful support from doctors in this country and overseas, but with a greater demand for first-aid classes we would gladly welcome further support to reduce the load upon those who help by lecturing and examining for us.—I am, etc.,

London, S.W.1. J. E. F. GUERITZ, Secretary, St. John Ambulance Association.

Unexplained Post-operative Reaction

SIR,—Over the last several months the McKellar General Hospital has had eleven severe immediately post-operative reactions consisting of pyrexia (temperature 105–107° F.—40.6–41.7° C.); transient granulocytopenia (a white blood count of less than 1,000 within a few hours of the reaction, later rising to about 30,000—98% polymorphs); severe shock requiring intravenous vasopressive drugs in high doses (up to 28 ml. "levophed" (noradrenaline)/litre for two to five days); mental confusion and agitation of a varying degree; followed by a marked eruption of herpes simplex lesion in the mouth, on the circumoral and malar areas in about two to three days. One was fatal. Only one patient received a blood transfusion. We believe that it may have been a pyrogenic intoxication or inhaled during the operative procedure (some as minor as a tooth extraction). Reactions which may have

had a similar aetiology have been reported following cardiac catheterization.[1 2] A septic abortion accompanied by a vascular collapse has been reported.[3] Detergents have been suggested as a vehicle.[4 5] However, no positive cause has been established in our cases.

Our hospital staff would like to know if other hospitals have experienced any similar reactions and what theories, facts, or leads may have been uncovered. Any reference to literature or personal reports of similar experiences would be appreciated by the undersigned. —I am, etc.,

McKellar General Hospital, Fort William, Ontario. G. H. MORRISON.

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3 Studdiford, W. E., and Douglas, G. W., *Amer. J. Obstet. Gynec.*, 1956, **71**, 842.
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Roundworms Wanted

SIR,—I am having difficulty in obtaining, for research purposes, specimens of the human intestinal roundworm *Ascaris lumbricoides*. I should be most grateful if any of your readers could supply me with any adult female worms, which they may find either in stools or at necropsy.—I am, etc.,

Department of Animal Pathology, School of Veterinary Medicine, Madingley Road, Cambridge. L. F. TAFFS.

POINTS FROM LETTERS

"Imferon"

Dr. R. DE SOLDENHOFF (Ayrshire Central Hospital, Irvine) writes: I think whoever wrote the leading article on "imferon" (March 12, p. 788) should have his head examined. While animal experiments are of importance in research, as stated, it is difficult to be sure that the same reaction will take place in the human being. In these days when the lay press will seize upon any snippet of medical information and broadcast it to the public, I think it is almost criminal to make a statement like that in the last paragraph without a good deal more investigation into the thousands of cases treated by imferon in the last five or more years. We ourselves use it a good deal in obstetrics, and so far no reaction of this nature has been noted.

Cardiac Arrest

Dr. M. G. BAGGOT (Great Falls Clinic, Montana, U.S.A.) writes: The point made by Mr. W. B. Fleming *et al.* (January 16, p. 157) that cardiac arrest does occur from a vago-vagal reflex is well taken. This disaster associated with foreign masses in the respiratory tract occurs in a variety of cases wherein drugs do not obscure the aetiology. . . . Most of the difficulties associated with relaxants arise from failure to block reflex stimuli. Hyporeactivity—i.e., obtundation of reflex mechanisms—is an essential part of good general anaesthesia. Incidentally, the probable explanation of the first episode was that the tube or the spray produced bronchospasm, which prevented alveolar exchange. Therefore the heart gradually became hypoxic. In another article Dr. L. Kaufman and co-authors (p. 166) discuss pseudocholinesterase deficiency, but its relevance to the case presented is questionable, since reflex apnoea was not excluded. The most likely cause of prolonged unconsciousness and respiratory arrest in this child was the tube, plus inadequate anaesthesia. Overdosage and respiratory obstruction are obvious hazards in general anaesthesia. For the rest, the following rule is helpful: until proved otherwise, all obscure phenomena in an anaesthetized patient are reflex effects due to some irritating mass in the respiratory passages, and the patient is (too) light.

Obituary

D. J. A. KERR, M.D., F.R.C.P.Ed.

Professor D. J. A. Kerr, professor of forensic medicine in the University of Edinburgh, died in Edinburgh on March 23. He was 65.

Douglas James Acworth Kerr was born at Bradford on August 21, 1894. He obtained his early education at St. Paul's School, London. Thereafter, following in the footsteps of his distinguished father, a pioneer in the school medical service, he took up the study of medicine. The first world war broke out while he was a student. Kerr immediately enlisted, was drafted to France in the Royal Artillery, and was wounded in September, 1914. Later he was attached to the Royal Flying Corps. Resuming his studies in Edinburgh in 1918, he graduated M.B., Ch.B. in 1920. Two years later he obtained the D.P.H., and in 1927 he proceeded M.D. with commendation. In the same year he was elected a Fellow of the Royal College of Physicians of Edinburgh, and at a later date became its treasurer, and for many years represented that institution on the General Medical Council.

He evinced an interest in forensic medicine soon after graduation, and became assistant to Professor Harvey Littlejohn in the University. He also helped him in the capacity of surgeon to the Edinburgh police, thus acquiring a first-rate knowledge of forensic medicine in its academic sense and also in its everyday application in police practice. When Professor Littlejohn died Dr. Kerr was appointed principal surgeon to the Edinburgh police and medical adviser to the Edinburgh Corporation. At the same time he obtained the appointment of lecturer in forensic medicine in the extramural school, a post which he held until the absorption of that body into the university.

When the regius chair in forensic medicine again became vacant in 1953 on the retirement of Sir Sydney Smith, the Crown appointed Kerr to the vacancy. He was the author of a very successful textbook on forensic medicine and contributed many papers to the scientific journals.

We are indebted to Sir SYDNEY SMITH for the following appreciation: The news of Professor Kerr's sudden death came as a great shock to his colleagues and friends, for, though he had suffered from coronary disease for some time, he appeared to be in good health until just before his demise. He held the regius chair in forensic medicine for only too short a time, his death coming seven years after his appointment.

Douglas Kerr was never a person who sought the limelight, but his retiring and modest disposition could not conceal his sterling character and medical acumen. He secured not only the affectionate regard of his medical colleagues but also the trust and respect of the police and judicial authorities with whom his work brought him into intimate contact.

We who knew him intimately will mourn the loss of a companionable, friendly colleague, and we extend to his widow and children our sincere sympathy.

J. B. MACALPINE, M.B., F.R.C.S.

Mr. J. B. Macalpine, the well-known genito-urinary surgeon and formerly honorary surgeon in charge of the genito-urinary department at the Salford Royal Hospital, died after a short illness at his home in Grasmere on March 17. He was 78 years of age.

James Barlow Macalpine was born on February 11, 1882, at Accrington, the son of Sir George W. Macalpine, LL.D. From Mill Hill school he went on to study medicine at Manchester University, graduating M.B., Ch.B. in 1907. After house appointments at Manchester Royal Infirmary he continued his postgraduate studies abroad, and took the

F.R.C.S. in 1910. Not long afterwards he was elected to the surgical staff of several hospitals in and around Manchester, including the Salford Royal Hospital, where he established and directed a genito-urinary department which was to become famous.

During the first world war he served in the R.A.M.C., and it was after his return to civilian life that he began to contribute important papers on urological subjects to this and other journals. A past-president of the Section of Urology at the Royal Society of Medicine, he was a Hunterian professor at the Royal College of Surgeons in 1947, and two years later he was awarded the St. Peter's Medal of the British Association of Urological Surgeons. At Manchester University he was honorary lecturer in urology, and in 1943 the university conferred on him the honorary degree of D.Sc. His book *Cystoscopy and Urography* was first published in 1927 and is now in its third edition.

Mr. CLIFFORD MORSON writes: The death of J. B. Macalpine has removed one more of a small band of surgeons who decided, 41 years ago, to devote the whole of their activity to the specialty of urology. In Lancashire A. H. Burgess, professor of surgery in the University of Manchester, had taken considerable interest in genito-urinary diseases, but he, like Wilson Hey at a later date, was essentially a general surgeon.

At Salford Macalpine developed a urological clinic which attracted postgraduates from far afield. It was a rewarding pleasure to be one of his guests, and after the operation session to dine with him and spend the rest of the evening playing billiards. His book on cystoscopy, the second of its kind to be written by a British urologist, proved a worthy successor to Hurry Fenwick's classic *Electric Illumination of the Bladder and Urethra*, published in 1888. Macalpine spent many exhausting hours at night writing his MSS., having no other time available. He once told me he wondered if it was worth while. Its success gave the answer.

From 1919 onwards Macalpine was an enthusiastic supporter of the Section of Urology of the Royal Society of Medicine. He was elected president in 1934. It gave him much pleasure to hear the president's address in October, 1959, given by his successor at Salford, Mr. D. S. Poole-Wilson. Macalpine was the first recipient of the St. Peter's medal presented to the British Association of Urological Surgeons by Bernard Ward of Birmingham. It is a sad reflection that only two of the members of the Urology Club which flourished before the second world war are alive to-day. Macalpine will be greatly missed by all his friends.

Mr. W. R. DOUGLAS writes: The death of James Barlow Macalpine must have come as a shock to his friends and to the world of urology. Jim, as he was called by his friends, was an athlete in his student days—a sprinter and a fine rugby back. He had an air of independence, slightly aloof, modest, rather shy, and not easy at first to know. He was something of an aristocrat—in fact he was a typical public-school product of the best type.

As often happens in the early medical years, men get together in small groups—in other words, men begin to "tune in" so to speak. Robert Ollerenshaw, Jim Macalpine, and I saw a good deal of each other. Macalpine devoted himself to urology and built up a department which has improved the status of Salford Royal Hospital and the like of which does not exist in any other Manchester hospital. I had hoped that one day when he was at his zenith he would have been absorbed by his teaching hospital—the Manchester Royal Infirmary—but it was not to be.

James Barlow was the son of wealthy parents, but this in no way militated against his progress—in fact, it enabled him to devote a great deal of his time to his specialty rather than to the establishment of a private practice. He was, as his name implies, a Scot. A hard worker, very thorough in all he did, he was always reaching out to the goal he had set himself. He was transparently honest and intolerant of humbug or slipshod work. Evidence of Macalpine's ability is seen in the world-wide reputation of his book and in the fact that his honorary degree of D.Sc. is an honour rarely bestowed on a Manchester surgeon.

In his later years the onset of bilateral Dupuytren's contracture in both hands prevented him from carrying on his technical surgical work and also deprived him of some of his hobbies. He was a gifted pianist, a good golfer with a low handicap, a yachtsman, and a billiards player.

This gifted surgeon, this dear friend and companion, has gone to his final rest, leaving a department which is a fine memorial to his work. He leaves a widow and family, to whom our deep sympathy goes out.

M. I. TOOHEY, M.D., M.R.C.P., D.C.H.

Dr. M. Toohey, medical consultant at New End Hospital, Hampstead, died in his hospital on March 21. He was 45 years of age.

Monty Toohey was born at Limerick on December 13, 1914. He was educated at Wesley College and Trinity College, Dublin, and he graduated M.B., B.Ch. in 1936, winning the Norman Connolly medal. He took the D.C.H. in 1938, and the M.R.C.P.(London) in 1939, and in 1941 he proceeded M.D.

Throughout the second world war he served with the R.A.M.C. in India, France, and the Far East, and was finally promoted to lieutenant-colonel in charge of a medical division. After the war Toohey became consultant physician to New End Hospital, and his main medical activities were centred at that hospital until his death.

The author of many articles in scientific and medical journals, he became widely known in recent years for his work on the treatment of coronary disease by anticoagulants and on methods of control. Several of his reports were published in this journal. In addition to these he wrote and had published a book, *Medicine for Nurses*, which has become a standard work and has already reached five editions. During his last four or five years Dr. Toohey was an enthusiast for the long-term treatment of atherosclerosis and coronary disease by means of anticoagulants, and this enthusiasm was responsible for the establishment at New End Hospital of a large and very well organized clinic. There is little doubt that his researches on anticoagulant treatment have increased knowledge about the precautions and safety factors concerned in the specialized treatment of coronary disease.

It was a little over three years ago that his health began to fail, and, although he had full knowledge that the condition was progressive and that he should have curtailed his activities in his clinic and research work, the fact instead spurred him on to still greater efforts. In addition, Toohey took a great interest in the activities of his hospital and was admired and respected by patients and staff. His loss to the hospital and medicine can hardly be gauged, although the results already obtained at his clinic must ultimately prove of the greatest value in the final evaluation of the treatment of coronary disease.

Dr. Toohey is survived by his widow and two daughters, and by his parents in Dublin. The sympathy of his friends is extended to them all.—J. E. P.

A. J. COUZENS, F.R.C.S.

Mr. A. J. Couzens, formerly senior surgeon to Queen Mary's Hospital for the East End, died on November 23, 1959, in a nursing-home at Hatch Beauchamp, Somerset. He was 89 years of age.

Alfred John Couzens was born on January 10, 1870. At the London Hospital, where he qualified in 1901, winning a surgical scholarship in the same year, he was resident receiving-room officer, assistant anaesthetist, and house-surgeon. He then moved to the West Ham Hospital (which later became the Queen Mary's Hospital for the East End) and was resident medical officer there for seven years.

Having taken the F.R.C.S. in 1907, he was elected to the honorary surgical staff not only of Queen Mary's Hospital but also of several other hospitals in east London. He had consulting-rooms in Wimpole Street, but for nearly all his professional life he lived in Romford Road, Forest Gate. Well known in the district, he was chairman of the Stratford Division of the B.M.A. from 1931 to 1933.

We are indebted to Mr. ALAN SMALL for the following appreciation: When I first met him, A. J. Couzens had been "Pa" Couzens for a long time, for it was 1933, the year after his retirement from the full surgical staff of Queen Mary's Hospital for the East End, which he had served for 30 years. For some years he continued to do a regular session or two, and eight years later emerged from a fuller retirement to become wartime casualty officer to the King George Hospital, Ilford, to which he had also been consulting surgeon from its foundation until 1932.

Couzens was a "London" man, and remained a loyal, though independent, son, living and working within the sphere of influence of his Alma Mater. In his early days at the West Ham Hospital he was a colleague of Frederick Treves, Jeremiah McCarthy, and Jonathan Hutchinson, junior, for to the East End the London Hospital was Athena, under whose aegis the local cottage hospital developed. These men's lives spanned from the antiseptic to the aseptic era, and Couzens, their disciple, though he lived and practised until so recently, accepted the change reluctantly and incompletely. It was quite an experience in 1933 to assist him to resect the bowel or remove the cartilage from a knee, using an antiseptic technique with considerable skill. Clad in a short-sleeved white coat, with maskless face and silver hair, bare hands, swabs, and instruments constantly bathed in lysoform, he not infrequently smoked a cigarette during the operation, while the theatre reeked of ether and steam from the fish kettle constantly boiling over an open flame.

He was an interesting character—a bachelor, a man who combined in a subtle and curious way the reticence and self-sufficiency of a shy individual with discriminating companionableness and sociability. He was admired, respected, and liked by his large circle of colleagues, with whom he was on the friendliest terms; he was an enthusiastic, though indifferent, golfer, and a car addict. He played a very full part in the social life of the hospital, and was a regular attender at hospital functions long after his official retirement, and these he enhanced with a lively and sometimes astringent wit.

Eighty-seven when he died at the end of last year, he had outlived most of the colleagues of his vigour by a generation. Among the survivors are Louis Welply of West Ham, for many years his best friend, and Sir Gordon Gordon-Taylor, who coached him for his Fellowship more than 50 years ago. To both of these I am indebted for help in the compilation of this memoir.

W. K. D. writes: I was once Mr. Cousens's house-surgeon and have many happy memories of him. He was always called "The Wise Man" at Queen Mary's Hospital for the East End, and it used to be a commonplace that, although he was rather an antiseptic as against an aseptic surgeon, the nursing staff always said that no one's wounds "did" so well as his. He seemed to love emergencies in the middle of the night, and was in his most pleasant and instructive form then.

R. SWYER, M.R.C.S., L.R.C.P., D.P.H.

Dr. Robert Swyer, who worked for many years in infectious diseases hospitals in North London, died in Crowborough Hospital, Sussex, on March 6. He was 70 years of age.

Born on November 3, 1889, the son of Dr. R. Swyer, who was a general practitioner at Wanstead, Essex, Swyer was educated at the City of London School and studied medicine at the London Hospital like his father before him. Just before qualification in 1912 he suffered from a severe illness which was thought to disable him from entering on a surgical career as well as preventing him from undertaking military service. Instead he became a ship surgeon for a time, an experience which he afterwards looked back upon with much pleasure. He joined the infectious diseases service of the Metropolitan Asylums Board in 1913 and was fortunate to work at the North Western Hospital, Hampstead, under the late Dr. E. W. Goodall, whose wide experience and great clinical acumen were at all times at the disposal of his junior colleagues.

From the first Dr. Swyer acquired a thorough grasp of the problems, administrative as well as clinical, which infectious diseases presented in those days, and achieved rapid promotion. When the M.A.B. hospitals were taken over by the London County Council in 1930 he was appointed deputy medical superintendent at the largest in London, then named North Eastern, and since 1948 St. Ann's General Hospital, where in due course he became consultant in his specialty, as well as honorary consultant to the Tottenham hospital group. He was lecturer in the University of London at the Royal Free and Middlesex hospitals, and at the London School of Hygiene and Tropical Medicine, for which he examined for the D.P.H. He was also a consultant in the diagnosis of smallpox for the Ministry of Health.

Numerous contributions to medical journals on clinical and, more recently, prophylactic problems appeared from his pen, all eminently sensible and practical; it is doubtful if any of his conclusions were subsequently proved to be invalid over the wide range he covered—especially anthrax, diphtheria, dysentery, and typhoid fever. In his early days surgery often had to be undertaken by the medical officer on the spot, and Dr. Swyer was particularly skilful at emergency tracheotomy. His precise and logical mind was combined with a caustic wit directed against principalities and powers rather than individuals. Indeed, he was fundamentally high-principled and kindly disposed to everyone with whom he came in contact, whether professionally or socially. After retirement he settled in the pleasant Crowborough district, where his hobbies of gardening, motoring, and photography were actively pursued to the end. In addition he was skilled in the domestic arts, especially the home brewing of wines, to the delight of his numerous friends.

He leaves a widow and a son, who is at present on the research staff of the Hospital for Sick Children, Toronto, and an assistant physician at the Toronto East General Hospital. They have our sincere sympathy.—W. G.

NORMAN BRIGGS, C.I.E., M.R.C.S., D.P.H.

The obituary of Colonel Norman Briggs was published in the *Journal* of March 26 (p. 973).

E. S. G. writes: I was very shocked to learn of the death of Colonel Norman Briggs, and I hope you will allow me, as one of his oldest friends, to supplement the obituary notice by a short pen-picture of his character and career as I knew him. Colonel Briggs, or Norman as he was known to his friends, was a most lovable man who by his innate modesty and charm, together with a strong sense of humour and a natural courtesy, endeared himself to all those with whom he came into contact. He was popular and respected by both Hindus and Mohammedans alike, for they realized full well that he was a man of integrity who could always be relied upon to give them a square deal. In addition to being a very human man and fond of his fellow creatures, he was also an extremely humane one, and the exercise of these qualities was largely responsible for his constant success in the posts which he held in the Indian Medical Service.

All the high and responsible positions to which Norman attained were won solely through his own efficiency, loyalty, and hard work, without pushing himself forward or seeking favours for his personal advancement.

Throughout his career he had the companionship and help of his wife, Molly, and I always considered them to be the beau-ideal of a happy married life. They were both fond of games and sport and enjoyed entertaining their friends.

One of their delights was in flowers, and the garden of their bungalow was always full of carefully tended flowers and shrubs of all kinds. It was no surprise to me to know that when they retired from India to Heathfield in Sussex they had taken up the growing of flowers and fruit professionally, and were making a success of it.

It is difficult to realize now that we shall not see Norman among us again. Though 68 years of age, he was always young in heart and enthusiastic in everything which he took up. He had such a joy in life that age counted little with him. His passing has left a terrible gap in the life of his widow, to whom we offer our deep sympathy.

THOMAS MULOCK-BENTLEY, L.R.C.P.&S.I.

Dr. Thomas Mulock-Bentley, one of the oldest doctors in South Africa, died in January at his home at Durban. He was 93 years of age.

Thomas Mulock-Bentley was born in 1866 in Dublin, where he received his medical education. He qualified L.R.C.P.&S.I. in 1888, and two years later settled in practice at Vrede, in the Orange Free State. On the outbreak of war in South Africa he was conscripted by the Boers and attended the wounded at the battle of Spion Kop. Later, on being released from the Boer forces, he joined the R.A.M.C., in which he attained the rank of major. For his services in the war he was mentioned in dispatches and awarded the Queen's medal, with four clasps, and the King's medal, with two clasps. During the first world war he served as a major in the South African Medical Corps. Dr. Mulock-Bentley enjoyed good health through his long life, and during the second world war he put on uniform once again and served as recruiting medical officer in Durban, where he had been in practice since 1925. He played tennis until he was well over 80, enjoyed a game of golf until a few years ago, and was a keen bridge-player. His wife died in 1957, and he is survived by three sons, one of whom, Dr. Thomas E. Mulock-Bentley, is in practice in Eshowe, Zululand.

A. A. BURRELL, M.B., B.Ch.

Dr. A. A. Burrell, formerly radiologist to the Isle of Wight County Hospital, died at Ryde on February 27. He was 80 years of age.

Arthur Ambrose Burrell was born at Kingstown, Ireland, on March 9, 1879. His early education was at Knutsford School in Cheshire, but he returned to Ireland to study medicine in the University of Dublin, where he graduated M.B., B.Ch. in 1902. After some years he took up radiology as a specialty and set up practice in Ryde, Isle of Wight, in 1912. During the first world war he served in the R.A.M.C., and worked in the 5th Southern General Hospital as radiologist. In addition to this and his own practice and hospital work he took on that of his friend, Dr. Beverley Bird, who was away on foreign service, and also the radiological work at the Royal Portsmouth Hospital. After the war he undertook most of the radiological work in the Isle of Wight. In 1928–9 he was chairman of the Isle of Wight Division of the B.M.A. At the onset of the second world war he became radiologist at Osborne House in addition to his civilian duties.

He retired from professional practice in 1946 owing to failing eyesight, and from then on devoted himself to the study of the classics, in which he was always deeply interested. He became something of a recluse, but those who were fortunate enough to enter his private sanctum were always enthralled by his erudition, his oratory, and his ready wit. Until his retirement he was an active mason, and was at his death the senior member of his Lodge. He was always interested in the progress of radiology and was at one time president of the Wessex branch of the British Institute of Radiologists.

He is survived by his wife, formerly Miss Rita Hesketh Biggs, a daughter, and two grandchildren.—L. F.-E.

Medico-Legal

CONSULTANTS' TAXES: TEST CASES

[FROM OUR LEGAL CORRESPONDENT]

Professional men who both hold an office and indulge in private practice may be in some difficulty when deducting expenses from income for the purpose of assessment for income tax. Gains from an office fall to be assessed under Schedule E, while gains from private professional practice fall to be assessed under Schedule D. The two schedules differ importantly in what are permissible deductions for expenses. Under Schedule E the permissible expenses are those wholly, exclusively, and *necessarily* incurred in the *performance* of the taxpayer's office or employment, while under Schedule D the permissible deductions are those wholly and exclusively expended for the purpose of the taxpayer's profession or vocation. The words *necessarily* and *performance* are literally interpreted, which makes a world of difference between the position of a man who pays tax under Schedule E (including all those who receive remuneration after payment of tax under P.A.Y.E.) and that of a man who is taxed under Schedule D.

In five test cases selected by agreement between the British Medical Association and the Inland Revenue an attempt has been made to settle the position of medical practitioners who hold appointments as part-time consultants under the National Health Service and also carry on private professional practice. The contribution made by private practice to total earnings differed considerably in each case. Is their income (and the expenses relevant thereto) to be split between Schedule E and Schedule D, or is it to fall wholly under one or the other? If so, under which of the two schedules?

On March 24 the Court of Appeal delivered judgment on appeals in these five cases, which were said to affect some 4,700 medical specialists (*The Times*, March 25). The five appellants were Dr. H. L. Ross, consultant radiologist; Dr. A. Hirtenstein, consultant ophthalmologist; Dr. A. G. Marshall, consultant pathologist; Dr. H. P. Tarnesby, consultant psychiatrist; and Mr. C. E. Drew, consultant thoracic surgeon. All these consultants held part-time appointments under the National Health Scheme during the relevant years of tax assessment. They all also had private patients.

Special Commissioners of Income Tax

All of the courts before which these cases have been heard so far have agreed in finding that the part-time appointments were "offices" within the meaning of Schedule E.

The first hearing was on the appeals by the five consultants to the Special Commissioners of Income Tax against the assessments. The Special Commissioners took a common-sense view of the appellants' mode of earning of a living, and upon this view held that the whole of their income fell under Schedule D. The Commissioners found as a fact that in the medical profession the normal way in which an individual becomes recognized as a consultant is by being appointed to the staff of a hospital. Before the introduction of the National Health Service such appointments were often honorary. After the introduction of the Service they were paid posts, but it remained the usual practice for part-time consultants to have a private practice apart from their hospital appointments. Both before and after the introduction of the Service the holder of an appointment on the staff of a hospital obtained definite advantages from it, both in the way of prestige and in more immediately practical ways. In those circumstances, the Special Commissioners held that the part-time appointments were a necessary part of the exercise of their

profession by the specialists and were merely incidental to it, and that earnings from those appointments fell to be assessed as part of their professional earnings under Schedule D. By this finding the Special Commissioners avoided the impossibly artificial task of allocating each item of expenses to one part or the other of the consultants' practice.

In Chancery

The Crown appealed from this finding to the Chancery Division of the High Court. Mr. Justice Upjohn, reversing the decision of the Special Commissioners, held that the fact that the exercise of an office under the National Health Service by a consultant might be described as an incident of the profession of a medical specialist was irrelevant. A specialist when carrying out his N.H.S. duties was performing the duties of a public office the profit or gains from which fell to be assessed under Schedule E; and when attending private patients he was exercising his profession, the profits or gains from which were to be assessed under Schedule D. Furthermore, said Mr. Justice Upjohn, when a specialist acted as a locumtenens in respect of an N.H.S. appointment he was for the time being performing the duties of the office of another, and the remuneration must therefore fall under Schedule D.

Consultants' Appeal Upheld

On appeal by the consultants, the Court of Appeal reversed the judgment of Mr. Justice Upjohn, and returned to a position somewhat similar to that adopted by the Special Commissioners.

The Special Commissioners had held that the specialists' remuneration from appointments fell under Schedule D. The Court of Appeal held that the remuneration from N.H.S. appointments fell to be taxed under Schedule E, but expenses (whether incurred in relation to appointments or in relation to private practice) could be deducted as a whole in the Schedule D assessment since they were expended for the purpose of the profession of consultant. In the section of the Income Tax Act, 1952, which allows deductions under Schedule D for expenses wholly and exclusively incurred for the purpose of the profession, the word "profession" could not be construed as meaning only that part of the profession the profits from which were taxable under Schedule D. "Profession" meant the whole profession, and the Court of Appeal agreed with the finding of fact by the Special Commissioners that, in the case of these consultants, their hospital appointments were a part of their profession.

Thus the law now is that consultants holding part-time National Health Service appointments can deduct all their expenses, no matter in which part of their practice they were incurred, from their Schedule D earnings and will be able to take advantage of the wider definition of permissible deductions under that schedule.

Reluctant Permission to go to Lords

However, leave to appeal to the House of Lords has been granted—"with the greatest possible reluctance," and their Lordships' decision remains to be seen. Moreover, it is not unlikely that our legislators may have read the unfavourable comments made by the judges of the Court of Appeal upon the historical anomaly which gives rise to the difference between the two schedules in the matter of expenses. Lord Justice Harman, for instance, remarked that it has been said that the pleasure of life depends nowadays upon the schedule under which a man lives. A statutory amendment may perhaps be made.

The Court ordered the Crown to pay two-thirds of the consultants' costs in both the High Court and the Court of Appeal. The remainder is being met from funds contributed principally by the Hospital Medical Staffs Defence Trustees and the medical defence societies. Messrs. Hempsons were solicitors for the consultants.

Medical Notes in Parliament

QUESTIONS IN THE COMMONS

Minister of Health Suggested for Cabinet

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Prime Minister on March 24 whether he would add the Minister of Health to the Cabinet, in view of the importance of the Health Service to the nation, and the admiration and interest shown in it by many other countries. Mr. HAROLD MACMILLAN pointed out that it was not possible to include in the Cabinet all Ministers in charge of Departments. "But (he said) it should not be inferred from this that the Government underrate the importance of the matters for which Ministers outside the Cabinet are responsible."

Dr. STROSS asked him to agree that it was difficult for observers abroad to appreciate that attitude; and to bear in mind also that the medical profession felt somewhat aggrieved on this matter. Could he give it some further attention? Mr. MACMILLAN replied that the composition of the Cabinet had always rested within the discretion of the Prime Minister of the day. Adjustments were made from time to time, but to some extent it was not desirable that the Cabinet should be too big, partly from the point of view of discussion and partly because of the character of the room in which they met.

Hospital Psychiatric Appointments

Mr. KENNETH ROBINSON (St. Pancras North, Lab.) asked the Minister of Health if he would state the number of consultants, senior hospital medical officers, senior registrars, and registrars holding hospital psychiatric appointments, at the latest date for which figures were available; and the percentages of the total number of doctors in each grade. Mr. WALKER-SMITH gave him the following information relating to the position at July 1, 1959:

Grade	No. of Hospital Psychiatric Appointments	Psychiatrists as Percentage of All Doctors in Grade
Consultants	645	9·4
Senior hospital medical officers	396	19·0
Senior registrars	135	12·7
Registrars	270	9·3

Radioactive Fall-out over Britain

Mrs. JOYCE BUTLER (Wood Green, Lab.) on March 22 asked the Minister of Health, as representing the Minister for Science, what was now believed to be the residence-time of fall-out in the stratosphere; and to what extent the figures of fall-out over Great Britain for the last few months or to the latest convenient date indicated that radioactive material was now virtually absent as a result of the voluntary suspension of hydrogen-bomb tests.

Mr. WALKER-SMITH stated that the time during which radioactive particles remained in the stratosphere after a nuclear explosion depended on the size, location, and time of year of the relevant nuclear explosion. The lowest estimates had varied from 15 months for material injected in equatorial regions in recent years to four months for material injected in Arctic regions in autumn, 1958. Measurements of radioactivity in air over the United Kingdom last autumn showed a very marked fall compared with earlier in the year, in part due to a seasonal decline. Measurements in the first half of 1960 were not yet available.

Doctors' and Dentists' Remuneration

Lord BALNIEL (Hertford, Con.) asked the Minister of Health on March 28 when he expected to be in a position

to announce his decision on the report of the Royal Commission on Doctors' and Dentists' Remuneration. Mr. WALKER-SMITH: The Secretary of State for Scotland and I are arranging to meet representatives of the professions in the near future for preliminary general discussions. I would hope to be able to make a statement to the House after these discussions.

Parental Consent to Treatment

Dr. DONALD JOHNSON (Carlisle, Con.) asked whether, in view of the breach of the long-established precedent that parents should be responsible for their children in all decisions concerning medical treatment which was involved in the action of the Sheffield Regional Hospital Board in establishing special juvenile courts in hospitals with powers to transfer responsibility to local authorities if parents refused permission for an operation on a child,* the Minister would request the board to postpone invitations to magistrates to set up such courts until the matter had been discussed on a national basis; and whether he would issue a White Paper with a view to promoting such discussion.

Mr. WALKER-SMITH stated that whether the provisions of the Children and Young Persons Act, 1933, would apply to a case of this kind, and what would be the effect of any order made under them, were questions of law on which it would not be appropriate for him to express any opinion. Accordingly he would not feel justified in intervening, and saw no reason to issue a White Paper on the subject.

Dr. JOHNSON asked what advice the Minister had given to the regional hospital board about Section 102 (1) of this Act, whereby parents were allowed an appeal to Quarter Sessions on a case such as this; and whether in his opinion it did not completely invalidate the procedure provided in these circumstances; and accordingly indicate that fresh legislation was necessary. Mr. WALKER-SMITH replied that he was sure the board were aware of the provisions of Section 102 in relation to appeals. The regional board were not seeking the use of any new powers in this context, but were merely trying to ensure that where the existing procedure was applicable it should operate speedily.

Smoking in Public Service Vehicles

Dr. ALAN THOMPSON (Dunfermline, Lab.) asked the Minister if he would consult with the Minister of Transport with a view to securing nation-wide acceptance of the principle that access to the lower decks of public service vehicles should be restricted to non-smokers in order to protect passengers, particularly older ones, suffering from chest complaints from the distress that might be caused by excessively smoky atmospheres.

Mr. WALKER-SMITH said he understood that the principle referred to was widely applied in practice. Bus operators naturally wished to satisfy their passengers, and the Minister of Transport and he thought it best to leave it to them and to the Traffic Commissioners to decide according to local circumstances.

Dr. THOMPSON asked what special medical knowledge the Minister of Transport had applied to the case in which he had more or less stated that the inhabitants of Durham who suffered from chest complaints were peculiarly immune to the effects of polluted atmosphere. What was required, and what was asked for by the County Councils' Association in a memorandum to the two Ministers, was the introduction throughout the country of a prohibition on smoking on the lower deck of double-deck vehicles. Mr. WALKER-SMITH said he understood that the Minister of Transport had allowed the appeal in the Durham case solely in the individual circumstances of that particular case. He accepted that in principle a ban on smoking could properly be made a condition of granting a route licence by the Traffic Commissioners. The Minister of Transport said he would certainly give due consideration to the county councils' recommendation.

*See *Brit. med. J.*, March 26, p. 943.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending March 12 (No. 10) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	1	1	0	1	5	0	3	0	
Dysentery	1,844	196	192	27	9	1,027	86	136	8	10
Encephalitis, acute	2	0	0	0		2	0		0	
Enteric fever:										
Typhoid	1	0	0	0	0	0	0	1	0	1
Paratyphoid	10	0	1	0	1	5	0	1 (B)	0	
Food-poisoning	193	26	3	5		126	27	4	1	
Infective enteritis or diarrhoea under 2 years				12	14				7	16
Measles*	2,141	90	83	5	36	22,733	1485	967	612	863
Meningococcal infection	25	4	6	0	2	28	2	8	1	1
Ophthalmia neonatorum	29	0	3	0		32	3	5	0	
Pneumonia†	501	29	203	14	8	2,039	100	535	29	33
Poliomyelitis, acute:										
Paralytic	6	0	0	0		11	0	3	0	
Non-paralytic	3	0	1			1	0	0		
Puerperal fever§	203	28	5	0		282	45	9	0	
Scarlet fever	1,077	34	59	16	24	1,240	63	47	27	18
Tuberculosis:										
Respiratory	455	38	62	6		637	52	88	11	
Non-respiratory	70	6	13	8		46	2	14	1	
Whooping-cough	782	49	171	10	30	585	21	59	51	113

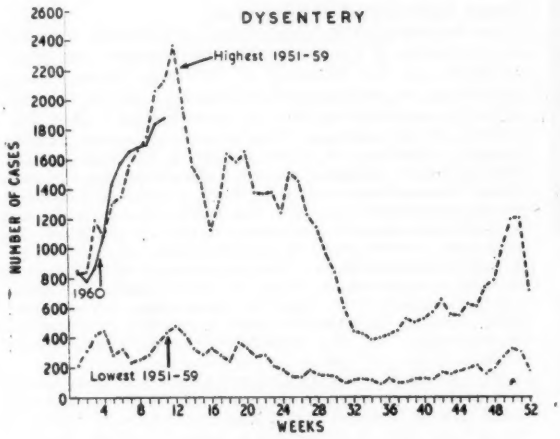
DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		3	0		0	
Encephalitis, acute					0		0			0
Enteric fever	0	0	0	0		1	0	0	0	
Infective enteritis or diarrhoea under 2 years	12	0	1	0	0	10	0	1	0	0
Influenza	35	1	1	1	0	907	35	29		8
Measles	0	0	0	0	0		0	2	0	0
Meningococcal infection		0	1				0	0		
Pneumonia	708	52	21	13	12	1,384	115	55	27	21
Poliomyelitis, acute	1	1		0	0	1	1		0	0
Scarlet fever	0	0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	89	3	9	0	4	121	11	7	1	7
Non-respiratory		3	0	0	0		0	1	0	1
Whooping-cough	1	0	0	0	0	1	0	0	0	1
Deaths 0–1 year	369	33	27	6	10	340	19	34	8	26
Deaths (excluding stillbirths)	11,119	880	619	136	215	13,560	1061	737	164	256
LIVE BIRTHS	15,574	1323	992	271	337	15,826	1410	1033	272	395
STILLBIRTHS	325	23	18			328	29	22		

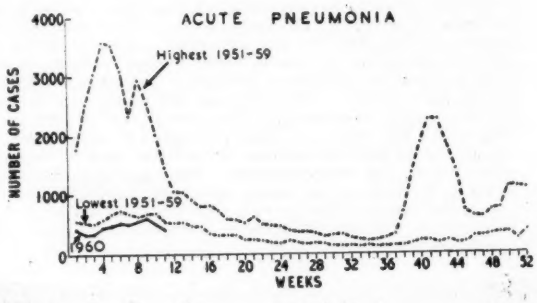
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia

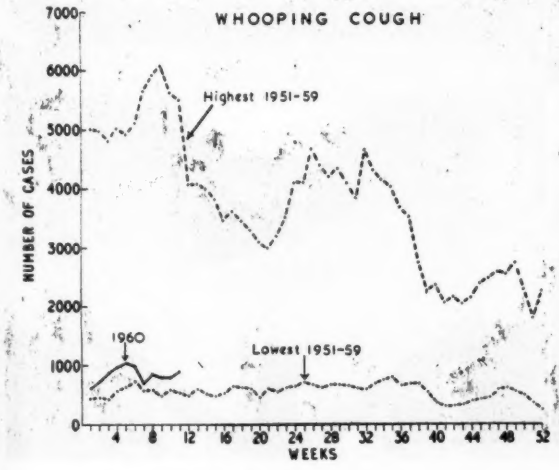
Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus - - - - - -, the figures for 1960 thus———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending Mar. 12	Week Ending Mar. 19
Dysentery		
Cheshire	64	**55**
Stalybridge M.B.	4	**17**
Devonshire	20	**30**
Exeter C.B.	6	**14**
Durham	42	**52**
Sunderland C.B.	0	**17**
Seaham U.D.	8	**18**
Gloucestershire	60	**58**
Bristol C.B.	45	**33**
Cirencester U.D.	4	**17**
Lancashire	454	**409**
Bolton C.B.	35	**22**
Liverpool C.B.	60	**43**
Oldham C.B.	55	**78**
Preston C.B.	50	**32**
Ashton-under-Lyne M.B.	27	**21**
Swinton and Pendlebury M.B.	54	**30**
Preston R.D.	10	**16**
West Lancashire R.D.	0	**12**
London	196	**192**
Camberwell	15	**14**
Islington	24	**20**
Southwark	38	**49**
Wandsworth	12	**18**
Norfolk	97	**70**
Norwich C.B.	47	**49**
Northamptonshire	12	**40**
Northampton C.B.	7	**20**
Nottinghamshire	43	**60**
Bingham R.D.	10	**24**
Suffolk	23	**27**
Ipswich C.B.	23	**23**
Wiltshire	38	**35**
Cricklade and Wootton Bassett R.D.	4	**20**
Yorkshire West Riding	155	**213**
Bradford C.B.	62	**36**
Huddersfield C.B.	12	**13**
Leeds C.B.	21	**53**
Sheffield C.B.	33	**58**
Rotherham R.D.	6	**23**
Glamorganshire	67	**48**
Ogmore and Garw U.D.	32	**23**
Monmouthshire	20	**34**
Abercarn U.D.	19	**25**
Glasgow	108	**108**
Dundee	5	**20**
Measles		
Dorsetshire	57	**136**
Sturminster R.D.	19	**65**
Northamptonshire	70	**119**
Desborough U.D.	18	**50**
Lancashire	544	**634**
Liverpool C.B.	134	**147**
Eccles M.B.	55	**128**

Influenza in England and Wales

During the week ended March 19 there were 33 deaths from influenza in England and Wales. Deaths from pneumonia, at 734, were slightly up on the previous week, and deaths from bronchitis, at 646, slightly down. Notifications of pneumonia, at 414, were lower than for several weeks past. Laboratory evidence of recent infection by influenza virus has again been found in a few cases.

Medical News

Royal College of Surgeons' New Laboratories

The new laboratories of the Royal College of Surgeons of England were opened on March 29. The QUEEN MOTHER could not be present because of illness, but Sir JAMES PATERSON ROSS read her speech at the official opening.

The new laboratories are, chronologically, phase 3a in the College's building programme, but they can be regarded in fact as an extension westwards of the Great Hall, museums, and laboratories of the first phase—the Nuffield College of Medical

Sciences representing the second. The new five-story building with its main facade facing on to Portugal Street includes—downwards floor by floor—an animal house; the department of anatomy; the department of ophthalmology—housing the Medical Research Council's Wernher group for research in ophthalmological genetics; the department of pathology; and the department of dental science—containing the odontological museum. The rotunda on the ground floor forms a striking setting for Weekes' statue of John Hunter, and the corridor leads westwards from there past the College's magnificent animal paintings by Stubbs, to committee rooms, the Fellows' room, and a lecture theatre. The building programme continues, the next stage including departments of pharmacology and of biochemistry, the Hunterian museum, a Rare Book Room for the library, and various offices and lecture rooms. The before-and-after picture shows the view between the columns as it is now—looking towards the new rotunda—and as it was nearly nineteen years ago after the raid of May, 1941. (Photograph of the bomb damage by courtesy of *The Times*.)

St. George's Hospital Medical School

St. George's Hospital has expanded steadily since it was first founded at Lanesborough House in 1733, and plans for a completely new building began in the years immediately before the second world war. However, even after the war, the way to rebuilding was not clear, and in 1954 the Board of Governors decided that, though a new St. George's was unlikely for at least 10 to 15 years, the buildings and facilities should not be allowed to deteriorate further. An interim building scheme was decided upon, and part of it—the medical school—has just been completed.

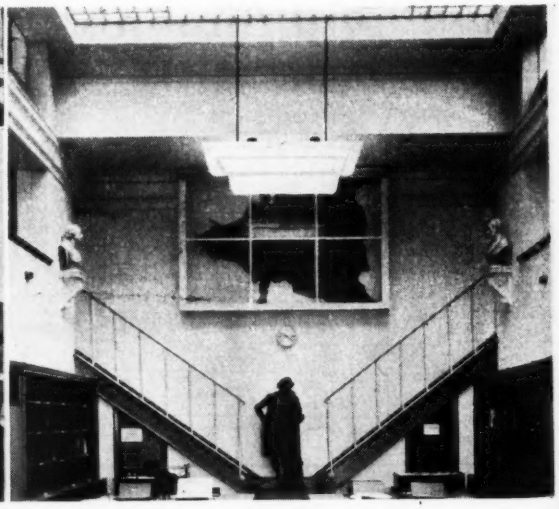
In effect, it links No. 9, Knightsbridge, with the existing school buildings to provide new laboratories for the departments of pathology, clinical pathology, bacteriology, and virology; clinical units in surgery and medicine; and improved lecture-room, library, and social facilities. The modernization plan involved the demolition of a great part of the school buildings, and the new library—complete with Jenner's famous cowhide—now stands on the site of what a 100 years ago was the dissecting-room. The group in the old photograph, taken on March 22, 1860, includes HENRY GRAY, of *Gray's Anatomy* fame. The other photograph shows the new library.

Prague Epidemiological Symposium

An International Epidemiological Symposium, organized by the Society of Czechoslovak Epidemiologists and Microbiologists on the initiative of Professor KAREL RAŠKA, director of the Institute of Epidemiology and Microbiology in Prague, was held in that city from February 22 to 26.

Eighty-six epidemiologists from 14 foreign countries attended, including eight from the United Kingdom. The majority, however, came from communist countries—Czechoslovakia, the Soviet Union, Poland, Bulgaria, East Germany, China, and Yugoslavia. Ninety papers were delivered in four and a half days, and, owing to axe-like chairmanship, there was even time for discussion. The main topics covered were: the concept and uses of epidemiology; the use of epidemiological methods in the study of non-infectious disease; epidemiological studies of acute respiratory disease, influenza, poliomyelitis, rheumatic fever, staphylococcal infections, infectious hepatitis, tick-borne encephalitis, ornithosis and toxoplasmosis; and the assessment of the effectiveness of vaccines.

The communist countries disagreed with the Western concept that epidemiology includes the study of the incidence in the community of non-infectious disease and wanted to restrict its use to "the study of chain-reaction diseases in which the link is a living organism." However, by the end of the week the conference agreed to a compromise statement which included the following paragraphs: "Epidemiology is a distinct discipline of medical science, concerned with the nature, cause, and spread of infectious diseases in the human population and using the knowledge so gained for the control, prevention, and eventual eradication of such diseases. This symposium has emphasized that the methods largely developed for the investigation of infectious diseases can be widely and effectively applied to other forms of disease and to different branches of medicine, such as hygiene, public health, and clinical medicine. This is particularly appropriate in the study of the factors influencing the distribution of these other forms of disease in human populations. As in the infectious diseases, this knowledge can lead to their control and prevention."



Editor: "Canadian Medical Association Journal"

Dr. D. C. GRAHAM, of Toronto, has been appointed editor of the *Canadian Medical Association Journal* from July 1. He succeeds Dr. S. S. B. GILDER, who relinquished the appointment a few weeks ago. During the interim period Dr. H. E. MACDERMOT, a former editor, will act as editor.

Dr. Graham is associate in medicine at the University of Toronto; physician-in-charge of the arthritis service, St. Michael's Hospital; a consultant to D.V.A. at Sunnybrook Hospital; and medical director of the Ontario division of the Canadian Arthritis and Rheumatism Society. He is a contributor to the "Year Book in Medicine."

Shortage of Midwives

The Association of Hospital Management Committees has sent a memorandum on the shortage of midwives to the Ministry of Health pointing out that there is no national shortage of pupil midwives, and that the shortage of trained midwives is the result of so many giving up midwifery after they have qualified.

The memorandum, quoting the figure of £600 given in a House of Commons debate on midwifery services as the cost of training a midwife, says that if this figure is accurate "it is a sobering thought that in a decade the money spent on training people for a profession they do not practise is equivalent to the allocation of capital monies for the Hospital Service in each of the first two years of nationalization." To avoid this waste of money and personnel the memorandum commends the incorporation—at present being discussed—of a short midwifery course in the basic nursing syllabus, and recommends that hospitals filling senior posts should not demand a midwifery qualification unless the job really calls for it.

New Nurse Training Regulations

A minimum educational qualification for entry to student nurse training is being introduced by the General Nursing Council, with the approval of the Ministry of Health, and it will come into force on July 1, 1962.

For students training to be general nurses, sick children's, and fever nurses, the requirement will be for General Certificate of Education at Ordinary level or an equivalent certificate in two subjects, of which one is English or Welsh language, with a full-time educational course of not less than five years and a satisfactory standard in five other subjects of general education. Overseas educational certificates of a similar standard are acceptable and alternatives include passing the Council's own test. The G.N.C. expects that one result of the new conditions will be to increase the number of training-schools for assistant nurses.

Oslo Summer School

A course on "Medical Care and Public Health Services in Norway" is being held at the Oslo University International Summer School in July this year (tentative dates July 2 to 29). Two grants of £45 each were available for British participants, and all applications should be sent to the International Summer School, 47, Karl Johansgt., Oslo, Norway.

The first two weeks will be taken up by lectures—in English—and excursions in Oslo. The remaining two will be spent in travelling to various parts of the country visiting public hospitals, maternal and child-health centres, diagnostic centres for tuberculosis, dental clinics, etc. The inclusive fee for lectures, accommodation, meals, and travel inside Norway is £119.

Ernest and Minnie Dawson Cancer Trust

A competition for a thesis on cancer by general practitioners has been announced by the Ernest and Minnie Dawson Cancer Trust, and up to £2,000 may be awarded in prizes. The competition, which closes on May 1, 1961, is open to doctors mainly engaged in general practice and who practise and/or reside in Lancashire, Yorkshire, Cheshire, Cumberland, Derbyshire, Durham, the Isle of Man, Lincolnshire, Northumberland, Nottinghamshire, or Westmorland. Details are given on advertisement p. 61.

Hypnotism Banned

The Market Research Society, which has for some time been investigating the use of hypnosis as a market research technique, has now revised its code of standards so that this technique is specifically banned. The basis of the Society's objection to its use is that it cuts across the individual's right to withdraw from the interviewing situation at any time either by refusing to answer a question or by terminating the interview.

Health Service Estimates

Civil estimates published on Tuesday provide a total of £519m. for the N.H.S. in the coming financial year. This includes £408.6m. for hospital running costs (a rise of £13.3m.), £69.5m. for general medical services (a rise of £3m.), and £66.9m. for drugs (a rise of £1m.). The estimates also include an additional £4.3m. for hospital building, bringing the total sum allocated for this to £25.5m. for the year. These estimates do not include provision for any increases in doctors' pay, and they relate to England and Wales only.

Health Service in Saskatchewan

The Saskatchewan College of Physicians and Surgeons has imposed a levy of $100 (over £37) a head on its members to provide a campaign fund—amounting to some $90,000—to fight the provincial government's health service plan which follows the British pattern. (*The Times*, March 28.)

Juvenile Delinquency in America

The Ford Foundation has given nearly £700,000 for a campaign against juvenile delinquency in the United States, and for studies on the subject to be carried out in several universities there. (*The Times*, March 24.)

Belgian Army M.O.s to Train Here

Selected medical officers in the Belgian Army are to spend part of their specialized training in the United Kingdom by arrangement with the British Council.

The scheme was inspired by Professor FERNAND ORBAN, professor of surgery at the University of Liége. Professor Orban escaped from Belgium in 1942, became a major in the Royal Army Medical Corps, and was awarded an honorary O.B.E.

Ultrasonic Microscope

The Paul Instrument Fund Committee has awarded £6,000 in supplement of a previous grant to Dr. C. N. SMYTH, of University College Hospital Medical School, London, and Mr. F. Y. POYNTON, of Northampton College of Advanced Technology, London, for the construction of an ultrasonic microscope.

The Paul Instrument Fund Committee was set up in 1945 "to receive applications from British subjects who are research workers in Great Britain for grants for the design, construction and maintenance of novel, unusual, or much improved types of physical instruments and apparatus for investigations in pure or applied physical science."

R.C.O.G.'s New Address

The Royal College of Obstetricians and Gynaecologists will be moving to their new building on April 2. Thereafter their address will be Sussex Place, Regent's Park, London, N.W.1 [AMB 5425].

New Westminster Dean

Dr. R. I. S. BAYLISS has been appointed dean of Westminster Hospital Medical School. He succeeds Mr. H. E. HARDING, who has resigned.

"Hospital Sepsis"

A film on infection in hospitals (produced under the direction of Dr. CARL WALTER of the Harvard Medical School in collaboration with the American Medical Association, the American College of Surgeons, and the American Hospital Association, with the support of Johnson and Johnson) is now available. By means of a particular case history, the film, "Hospital Sepsis—a Communicable Disease," states afresh the basic principles involved in the spread of infection. Inquiries about the film should be addressed to Mr. M. A. ADBURGHAM, Johnson and Johnson, Ltd., Slough, Buckinghamshire.

Oliver Bird Prize

The Oliver Bird Prize for 1959 has been awarded to Miss H. M. BRUCE, B.Sc., of the National Institute for Medical Research, London, for a series of papers submitted under the general title of "An Exteroceptive Block to Pregnancy."

COMING EVENTS

N.W. England Faculty, College of General Practitioners.—It is regretted that no further applications can be accepted for the symposium on "Chronic Bronchitis in General Practice." (*Journal*, March 19, p. 891.)

W.H.O. Exhibition.—Exhibition on work of W.H.O. to celebrate World Health Day (April 7), Charing Cross Underground Station exhibition site, April 4–23. Open daily, except Sunday, 11 a.m.–7 p.m. (Closed Good Friday.)

Haemophilia Society.—Annual general meeting, April 10, 3 p.m., The Hospital for Sick Children, Great Ormond Street, London, W.C.1.

British Association of Physical Medicine.—Annual meeting, April 29–30, at King's College Hospital, Denmark Hill, London, S.E.5. Details from B.A.P.M., 47, Lincoln's Inn Fields, London, W.C.2.

Canadian Thoracic Society.—Annual meeting, Ottawa, June 27–30, in conjunction with 60th Jubilee meeting of Canadian Tuberculosis Association. Details from Dr. C. W. L. JEANES, Canadian Thoracic Society (Medical Section of the Canadian Tuberculosis Association), 265, Elgin Street, Ottawa, 4, Canada.

NEW ISSUES

*The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.*1.

BRITISH JOURNAL OF OPHTHALMOLOGY.—Issued monthly (£6 annually). The new issue (Vol. 44, No. 2) includes:

Experimental Trachoma Produced by Cultured Virus. Part II. L. H. Collier, S. Duke-Elder, and B. R. Jones.
Pilot Study in Electro-Oculography. B. Shackel.
Peripheral Iridectomy in Closed-Angle Glaucoma. P. L. Baxter and S. Chatterjee.
Bilateral Secondary Glaucoma and Systemic Hypertension in Marfan's Syndrome. V. A. F. Martin and E. C. Cowan.
Book Reviews.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, April 3

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Radiotherapeutic Centre, Addenbrooke's Hospital, 2.15 p.m., (1) Mr. O. Lloyd: Diagnosis and Treatment of Vaginal Discharge; (2) Mr. S. J. Hopkins, Ph.C., M.P.S.: An Assessment of Vaginal Therapeutic Preparations. 3.15 p.m., Mr. J. Carron Brown: The Underprivileged Breech; 4.15 p.m., Dr. Janet Bottomley: Carcinoma of the Uterus.

Monday, April 4

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—6 p.m., Professor L. B. W. Jongkees (Amsterdam): Physiology of the Static Labyrinth.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor J. H. Hovell: Surgical Treatment of Mandibular Prognathism, with Special Reference to Functional Anatomical Considerations in Diagnosis and Treatment Planning.
ROYAL SOCIETY OF HEALTH.—At Caxton Hall, Westminster, London, S.W., 2.30 p.m., Dr. M. G. Candau (Director-General, W.H.O.): Public Health Education in Relation to Atomic Energy and Radiation Hazards; Training of Local Authority and Other Appropriate Personnel.

Tuesday, April 5

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Lumleian Lecture by Dr. D. E. Bedford: Disorders of the Pulmonary Circulation.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Ophthalmology Lecture by Professor A. Sorsby: Blindness in Children: Genetic Aspects.

Wednesday, April 6

FOUNTAIN HOSPITAL.—5.30 p.m., films: (1) Embryology of Human Behaviour; (2) Life Begins in Leeds.
MIDLAND MEDICAL SOCIETY.—8.15 p.m., annual general meeting. Dr. Philip H. Addison (Medical Defence Union): Legal Pitfalls of Medical Practice.
ROYAL COLLEGE OF SURGEONS OF ENGLAND AND INSTITUTE OF UROLOGY.—At Royal College of Surgeons of England, 5 p.m., Urology Lecture by Mr. R. A. Mogg: Renal and Ureteric Neoplasms.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. Peter McIntosh, M.A.: Sport and Society.

Thursday, April 7

BELMONT HOSPITAL CLINICAL SOCIETY.—8 p.m., Dr. A. Russell Lee: Intrafamilial Environment of the Schizophrenic.
BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Dr. D. McC. Gregg, Dr. K. E. Jefferson, Dr. R. E. Steiner, and Dr. David Sutton: Thoracic Aortography.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Lumleian Lecture by Dr. D. E. Bedford: Disorders of the Pulmonary Circulation.

Friday, April 8

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, University College, Gower Street, W.C., 10.25 a.m., 393rd meeting (annual general meeting).
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Professor F. C. Ormerod: Classification and Grading of Cancer of Larynx and Pharynx.
INSTITUTE OF NEUROLOGY.—4.30 p.m., Dr. P. W. Nathan: Nerve Fibres Subserving Cutaneous Sensation.
KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.
SOCIETY OF MEDICAL OFFICERS OF HEALTH: SERVICES GROUP.—At Committee Room C, B.M.A. House, Tavistock Square, W.C., 5.30 p.m., Presidential Address by Dr. J. Craig Lindsay: One Hundred Years of Civil, Military, and Medical Co-operation.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal Society of Arts, 8.30 p.m., Cavendish Lecture by Sir David Campbell: Some Observations on the History of the Treatment of Disease.

Saturday, April 9

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Lecture Room "B," Addenbrooke's Hospital, Cambridge, Symposium on Gastro-intestinal Diseases. *Morning*: 10.30 a.m., Dr. D. Russell Davis: Functional Dyspepsia; 11.30 a.m., Mr. K. F. Wilsdon: Dysphagia; 12.15 p.m., Dr. F. R. Berridge: The Gastro-oesophageal Junction. *Afternoon*: 2.15 p.m., Dr. A. P. Dick: Malabsorption Syndromes; 3 p.m., Dr. J. M. Walshe: Jaundice; 4 p.m., Mr. J. F. R. Withycombe: The Surgical Treatment of Ulcerative Colitis.
INSTITUTION OF HOSPITAL ENGINEERS.—At Meyerstein Memorial Lecture Theatre, Westminster Hospital Medical School, Horseferry Road, S.W., 2.30 p.m., Sandford Premium Lecture by Dr. L. R. West; Some Engineering Principles in Medicine (illustrated).
SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Preston Hall Chest Hospital, near Maidstone, Kent, 10.30 for 11 a.m., Sir Clement Price Thomas: Carcinoma of the Lung.

Sunday, April 10

KING'S COLLEGE HOSPITAL.—At Out-patient Department, 10.30 a.m. to 12.30 p.m., clinical meeting for general practitioners.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Stewart.—On March 18, 1960, at St. Mary's Hospital, Manchester, to Margaret (formerly Hinmers), and Dr. J. G. Stewart, a son—Rory William.

DEATHS

Anderson.—On March 8, 1960, in hospital, Hamish Morton Anderson, M.B., F.R.C.S.Ed., of 3, Prince of Wales Terrace, London, W.
Banks.—On March 7, 1960, Alexander Grey Banks, M.D., F.R.C.S.Ed., of Fairfield Close, Lymington, Hants, late of Ipswich, Suffolk.
Barford.—On February 23, 1960, at "Home," Bridgeway, Selsey, Sussex, Percy Crompe Barford, M.B., aged 91.
Bates.—On March 14, 1960, George Llewellyn Bates, M.R.C.S., L.R.C.P., L.D.S., of Sidcup, Kent, aged 87.
Biggam.—On March 9, 1960, in a nursing-home, Edinburgh, James Biggam, *M.C.*, M.B., Ch.B., D.O.M.S., colonel, late R.A.M.C., retired, of "Seaforth," Broadstone Road, Stranraer, Wigtownshire.
Birkett.—On February 21, 1960, at 2, Highbury Hall, Weston-super-Mare, Som., Jane Louisa Jarrett Birkett, M.D., aged 94.
Bulman.—On February 17, 1960, in hospital, John Roderick Bulman, M.B., Ch.B., of 20, Aylestone Hill, Hereford, aged 74.
Cogan.—On March 4, 1960, in hospital, Edinburgh, William St. John Cogan, L.R.C.P.&S.Ed., L.R.F.P.S., J.P., of 11, Hermitage Place, Leith, Edinburgh.
Dadachanji.—On March 6, 1960, at University College Hospital, London, W.C., Rustom Kershasp Dadachanji, F.R.C.S.Ed., of 389, City Road, London, E.C.
Dixon.—On March 16, 1960, Thomas Benjamin Dixon, C.B.E., V.R.D., M.R.C.S., L.R.C.P., surgeon captain, R.N.V.R., retired, of Avon Cottage, Bantham, Kingsbridge, Devon, formerly of Bristol, aged 74.
Dunlop.—On March 14, 1960, in hospital, James Alistair Dunlop, M.B., Ch.B., D.P.H., of 476, Normanby Road, Normanby, Middlesbrough, Yorks.
Elliott.—On March 14, 1960, at his home, 5B, Elton Road, Bristol, William Harold Arthur Elliott, M.B., B.S., aged 82.
Errington.—On March 14, 1960, Roger Errington, C.B.E., *M.C.*, T.D., M.D., colonel, A.M.S., retired, of West Avenue, Gosforth, Newcastle upon Tyne, Northumberland.
Ford.—On March 12, 1960, at 21B, Devonshire Place, London, W., Harriet Rosa Delo Ford, M.B., D.O., aged 86.
Granger.—On March 10, 1960, in hospital, Edgar Granger, M.B., Ch.B., of The Willows, Shabbington, Bucks.
Granger.—On March 14, 1960, at his home, Tudor Grange, Gervis Road, Bournemouth, Hants, Henry Granger, M.R.C.S., L.R.C.P.
Holland.—On March 6, 1960, in London, Roger Oswald Holland, M.R.C.S., L.R.C.P., L.D.S.
Jack.—On March 11, 1960, in hospital, Frederick Joseph Jack, L.R.C.P.& S.Ed., L.R.F.P.S., of 11, Hillcrest Road, Little Sutton, Cheshire.
Klein.—On March 4, 1960, at Dumfries Infirmary, Robert Klein, M.D., aged 64.
Lees.—On March 17, 1960, Joseph Montagu Lees, B.M., B.Ch., D.M.R., of Askham Bryan, Yorks.
Macalpine.—On March 17, 1960, at Michael's Nook, Grasmere, Westmorland, James Barlow Macalpine, D.Sc.(Hon.), M.B., F.R.C.S., aged 78.
Pillans.—On March 7, 1960, at 14, Kingsborough Gardens, Glasgow, George Lynn Pillans, *M.C.*, F.R.F.P.S., L.R.C.P.&S.Ed.
Saunders.—On March 15, 1960, at Napsbury Hospital, St. Albans, Herts, Benjamin Theodore Saunders, M.B., Ch.B., D.P.H., late of Amulree House, Church Road, Bolton, Lancs.
Sewell.—On March 15, 1960, David Lindley Sewell, M.B., B.S., late of Manchester, aged 81.
Simpson.—On March 8, 1960, at Edinburgh Royal Infirmary, James McDonald Simpson, M.B.E., M.D., D.P.H., of 96, Liberton Drive, Edinburgh.
Stanley.—On March 16, 1960, at North Thoresby, Grimsby, Lincs, George Wheldale Stanley, *M.C.*, L.R.C.P.&S.I. & L.M., aged 74.
Thomson.—On February 16, 1960, James Robert Karran Thomson, O.B.E., M.R.C.S., L.R.C.P., of Thorpe Tirril, Penrith, Cumberland, aged 69.
Ward-Smith.—On March 14, 1960, at the Duke of York Home, Bradford, Yorks, Ward Ward-Smith, M.D., F.R.C.S., of 10, Sherwood Grove, Shipley, Yorks, aged 84.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Dermatological Side-effects of Phenindione

Q.—*Are there any known dermatological side-effects attributable to the prolonged use of phenindione ?*

A.—When discussing side-effects of drugs it is important to differentiate, if possible, between reactions due to overdosage and direct toxic effects and those due to allergic manifestations. In the former group of reactions the clinical manifestations of toxicity will vary little from patient to patient and they will be closely related to the dosage, while allergic reactions, the result of an immunological process, show marked individual variation and can be induced by very small quantities of the sensitizing drug. It is impossible to detail here all dermatological side-effects which have been attributed with good reason to the prolonged use of any anticoagulant drug, but pruritus, maculo-papular rashes, and transient alopecia have been noted as rare complications during treatment with a number of these preparations. Phenindione has been used widely since 1947, although its sensitizing faculties became evident during early clinical trials and Soulier and Gueguen[1] reported in that year transient mild rashes in two patients during treatment. At least 15 other reports have been published of various side-effects of phenindione, including the following dermatological manifestations: pruritus, urticaria, morbilliform and maculopapular eruptions, as well as ulceration of the oral mucosa.[2–7] The literature of phenindione sensitivity has been reviewed by Burns and Desmond[3] and Bingle and Shine.[8] While Toohey[9] found the incidence of mild transient rashes during treatment with phenindione to be 1–2% at the New End Hospital, London, Ager and Ingram[10] did not report any skin lesions in a review of 900 patients treated with the same drug at St. Thomas's Hospital, London.

REFERENCES

1 Soulier, J. P., and Gueguen, J., *C.R. Soc. Biol. (Paris)*, 1947, **141**, 1007.
2 Brown, K. W. G., and MacMillan, R. L., *Amer. J. med. Sci.*, 1954, **227**, 526.
3 Burns, C., and Desmond, F. B., *N.Z. med. J.*, 1958, **57**, 283.
4 Johnman, L., *Scot. med. J.*, 1957, **2**, 330.
5 Kirkeby, K., *Lancet*, 1954, **2**, 580.
6 Makous, N., and Vander Veer, J. B., *J. Amer. med. Ass.*, 1954, **155**, 739.
7 Mayer, A. C., *Lancet*, 1954, **2**, 708.
8 Bingle, J., and Shine, I., ibid., 1959, **2**, 377.
9 Toohey, M., *Brit. med. J.*, 1953, **1**, 650.
10 Ager, J. A. M., and Ingram, G. I. C., ibid., 1957, **1**, 1102.

Lymphosarcoma in the Family

Q.—*A 9-year-old boy died recently from lymphosarcoma. A maternal uncle died from the same disease at the same age. The parents want another child. What are the chances of this child developing lymphosarcoma ?*

A.—There is little chance that a further child born in this family will develop lymphosarcoma. It is most unusual to find two relatives both affected with lymphosarcoma.

A Drug for Paralysis

Q.—*It is reported in the newspapers that the Russians have discovered a drug called "karantonim," derived from an Asiatic plant called karkauak, or black globule, which is said to cure the paralysis caused by poliomyelitis. Is anything known about this drug, and is it likely that any drug to cure paralysis might be found ?*

A.—This report does not sound as though it had come directly from a scientific institute, for everyone knows that there is no possibility of established paralysis in poliomyelitis being cured, owing to the fact that the nerve cells have disappeared and no replacement can occur. It is, of course, possible that a drug might be found which would interfere with the death of the cell during the acute stage of the disease, but any such drug if really effective would be shown to have this effect in the experimental poliomyelitis. This would be a very dramatic discovery, which we would be unlikely to hear about in the first place from a rather vague newspaper report. On the whole, therefore, it sounds like one of the innumerable claims connected with poliomyelitis that have been made in the past and which time shows to be without foundation.

Vasomotor Changes in Peripheral Neuritis

Q.—*In cases of peripheral neuritis I have seen vasomotor changes characterized in some cases by vasoconstriction (cold limbs) and by vasodilatation in others. What is the explanation of this ?*

A.—In patients with chronic lower motor neurone lesions cold limbs are common, probably resulting from disuse of the limb. This may occur in peripheral neuritis as well as in patients who have had anterior poliomyelitis. In some cases of peripheral neuritis, however, perhaps more especially when this is due to diabetes mellitus, sympathetic fibres may be affected with resulting vasodilatation.

Snuff-taking

Q.—*Is there any evidence that snuff-taking is harmful ?*

A.—The active ingredient of most forms of snuff other than medicinal snuffs is powdered tobacco. The persistent snuff-taker therefore, like the persistent smoker, becomes addicted to nicotine. In the sense that addiction to any drug is undesirable this may be claimed to be a harmful effect of snuff-taking. Apart from this, however, there is little evidence that snuff-taking is injurious to health. It is claimed that it may interfere with the sense of smell by damaging the filaments of the olfactory nerve and also that it may cause changes in the nasal mucous membrane. In view of recent evidence establishing a connexion between smoking and bronchial carcinoma one wonders whether persistent snuff-taking might be associated with an increased incidence of malignant disease of the upper respiratory tract, but the writer knows of no evidence that this is the case.

Nail-biting

Q.—*A 16-year-old girl is a nail-biter. Otherwise she does not seem to be unduly nervous. Bitter aloes and other treatments have failed. Should hypnosis be tried ?*

A.—Before recommending hypnosis as a form of therapy for a persistent nail-biter it would be necessary to know much more about the case—e.g., who is motivated to stop this symptom, parents or girl; is the absence of signs of "nervousness" due to the canalization of anxiety into the one symptom of nail-biting; is the symptom of nail-biting giving such emotional satisfaction that the "habit" aspect is of relatively little importance, so that bitter aloes, etc., have failed to modify it ? The symptom might well be removed by hypnosis, but this could be not only undesirable (all symptoms serve a useful purpose of some sort) but even dangerous if used before the diagnosis has been established.

Mumps Encephalitis

Q.—*What is the incidence, diagnosis, course, prognosis, and treatment of encephalitis complicating mumps ?*

A.—It is impossible to assess the exact incidence of encephalitis in mumps since there is no way of estimating the incidence of mumps itself. In one outbreak in Gurkha troops the incidence of meningo-encephalitis was 6.3%,[1] but this is probably much higher than in Britain. In the differential diagnosis of lymphocytic meningitis, when poliomyelitis and tuberculous meningitis have been excluded, mumps is probably the next most likely cause. Diagnosis when there is a history of preceding parotitis is easy, but when there is none acute and convalescent specimens of blood should be taken for serological examination: there is usually a sharp rise in titre. History of contact often

gives the clue, as in an adult developing meningo-encephalitis in a family in which a child had recently had parotitis. The course of the disease is usually relatively mild, but sometimes the patient is comatose. Recovery is usually obvious after a few days to a week and the patient is well within a fortnight. There is no specific treatment. Cortisone has been used, but with doubtful success[2]: since spontaneous recovery is the rule, there seems no need to use it except in unusually severe cases.

REFERENCES

[1] Russell, R. R., and Donald, J. C., *Brit. med. J.*, 1958, **2**, 27.
[2] Spitznagel, J. K., *Ann. intern. Med.*, 1958, **49**, 61.

Lung Cancer in Non-smokers

Q.—*What increase, if any, has there been in the incidence of lung cancer among non-smokers in the past few years?*

A.—Observations on non-smokers have not as yet been made for a sufficient number of years to provide any direct indication of whether there has been an increase of lung cancer among non-smokers. The observations are difficult to make because the condition is rare and large numbers need to be studied. Estimates of the incidence among non-smokers are higher than the mortality from lung cancer recorded for all persons before about 1935, but there seems little doubt that the early mortality figures substantially underestimated the true incidence. There is some evidence to suggest that the incidence among non-smokers is somewhat higher in large towns than in the countryside (perhaps about two to three times greater[1]), and, although the evidence is not all consistent,[2] it is reasonable to suppose that some real increase may have occurred among non-smokers. If it has, it is unlikely to have been large.

REFERENCES

[1] Stocks, P., *Annual Report of the British Empire Cancer Campaign for 1957*. Supplement to Part II, p. 78.
[2] Doll, R., in *Carcinoma of the Lung*, 1958, edited by R. Bignall, p. 88. Livingstone, Edinburgh.

Herpes Simplex of the Cornea

Q.—*What is the treatment of herpes simplex of the cornea?*

A.—Although some cases of keratitis due to herpes simplex run a self-limiting course without treatment, others may persist or recur for many months with ultimate blindness or loss of the eye.

The crucial point in treatment is the removal of virus-invaded epithelium and gentle application of a virucidal agent such as iodine, phenol, or ether as early as possible. Atropine is needed. No known antibiotic or chemotherapeutic drug is effective against this virus, and they can do no more than discourage secondary infection.

Steroids may be of value if a stromal or disciform keratitis supervenes, but they increase the danger of recurrence of virus proliferation in the epithelium—furthermore, they mask the symptoms and some of the attendant signs. Such a recurrence must be dealt with by local removal, but, even so, it may damage the eye very severely. Steroids are thus a two-edged weapon, and should only be used in selected cases under the most careful and expert supervision. Some authorities consider that they should never be used in this disease. Therapeutic lamella grafting is very valuable in severe deep herpetic keratitis.

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Thygeson, P. Kimura, S. J., and Hogan, M. J., *A.M.A. Arch. Ophthal.*, 1956, **56**, 375.
Jones, B. R., *Trans. Ophthal. Soc. U.K.*, 1959, **79**, 425.

Early Rising After Labour

Q.—*Why do gynaecologists favour early rising after surgery, but still tend to keep obstetrical cases in bed long enough to cause loss of muscle tone?*

A.—The questioner's point is not accepted. Early rising after labour was preached as long as 60 years ago, and was commented on in the columns of the *Journal* 10 years ago.[1] In nearly every maternity unit to-day the patient is encouraged to sit out of bed the day after delivery (even after caesarean section) and thereafter the range of movement is extended daily.

REFERENCE

[1] *Brit. med. J.*, 1950, **1**, 948.

Probability of Death of Doctors

Q.—*A table in the Government Actuary's report on the N.H.S. Superannuation Scheme*[1] *shows that the probability of death is on average 50% greater between the ages of 52 and 65 in medical and dental practitioners than in other workers in the Health Service. What might be the explanation of this, and does it reflect the position of practising doctors vis-à-vis the population as a whole?*

A.—The table referred to by the questioner relates only to the probability of death *in service* and does not take into account the deaths of those persons who had retired—for whatever reason—and then died. The groups compared with the medical and dental practitioners contain manual and other relatively unskilled workers. Members of this last group—particularly the manual workers—who are unable to maintain their normal efficiency are forced completely to sever their connexion with the service, even though they may take another lighter job elsewhere. A doctor, on the other hand, is always a doctor and will usually remain at work in the National Health Service even though he may ease off. This state of affairs will result in a higher mortality for doctors in service than for other workers in service. In other words, the data, while true so far as they go, should not be used to generalize about the mortality of doctors *vis-à-vis* the mortality of other workers.

This is borne out by a comparison of the data in this table with those given in the English Life Table No. 11,[2] which shows that the probability of a doctor or dentist dying in service is less than that of the male population as a whole. Perhaps a better comparison is provided by the Registrar-General.[3] This shows that at 55–64 the death rate of medical practitioners was 92% of that for all males; for dental practitioners the ratio was 101%.

REFERENCES

[1] *Report of the Government Actuary on the National Health Service Superannuation Scheme, 1948-1955*, 1959, p. 21. H.M.S.O., London.
[2] Registrar-General, *Decennial Supplement England and Wales, 1951*, 1957, Life Tables. H.M.S.O., London.
[3] Registrar-General, *Decennial Supplement of England and Wales, 1951*, 1958, Occupational Mortality, Part II. H.M.S.O., London.

Corrections.—The approved name of "glucophage" (*Brit. med. J.*, March 12, page 798) should have been given as metformin, not methformin.

In the article on "Paediatric Prescribing" by Professor W. Gaisford (March 12, page 794) we regret that the equivalent of 0.5 mg./lb. was incorrectly given as 0.1 instead of 1.0 mg./kg.

The letter on "Mid-stream Urine from Women" (March 26, p. 961) was wrongly attributed to Dr. Elizabeth C. Wood and others. The attribution should have been to Mr. Edwin C. Wood.

The date of death of Dr. Wu Lien-Teh was wrongly given in the obituary notice printed in the *Journal* of February 6 (p. 429): he died on January 21, 1960.

In the paper on "Sedatives for Children" (March 19, p. 871) Professor R. S. Illingworth stated that thalidomide ("distaval") costs about forty times more than chloral. In fact, one tablet of thalidomide (25 mg.) would cost (at hospital prices) approximately thirteen times more than 7½ gr. of chloral.

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